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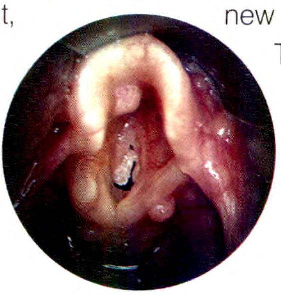

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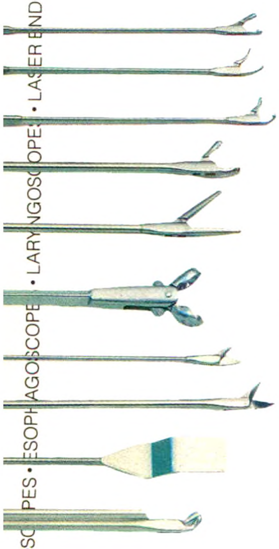

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Closing date for applications is April 15, 1991.

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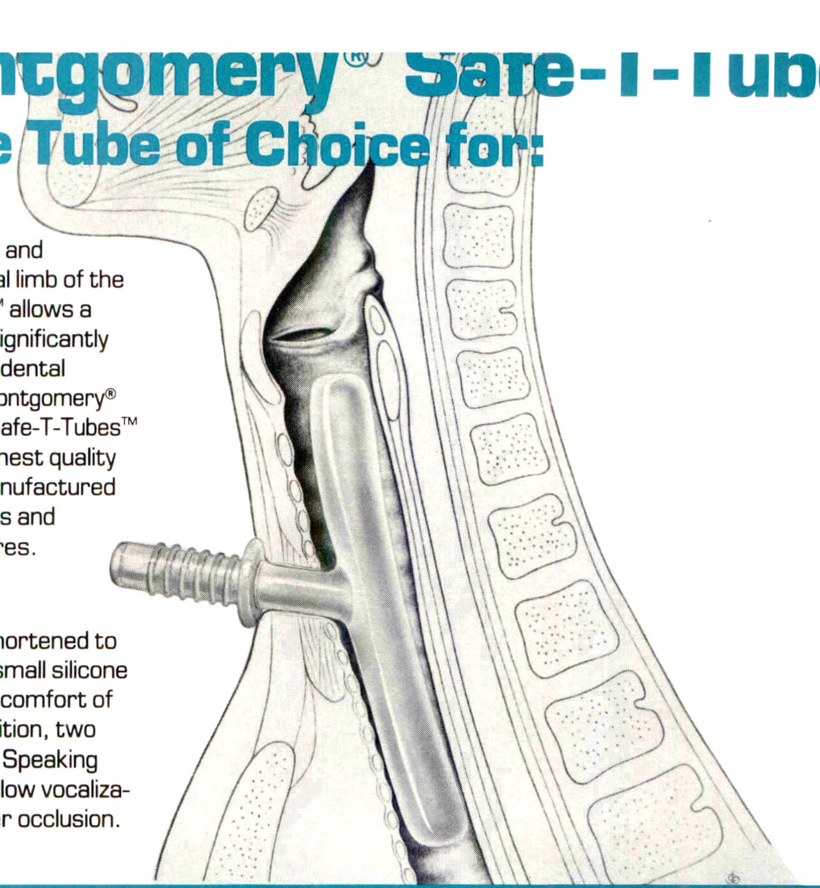

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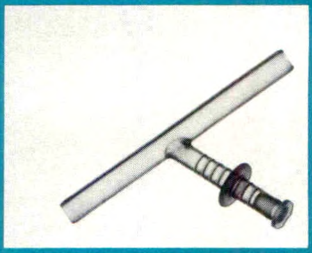

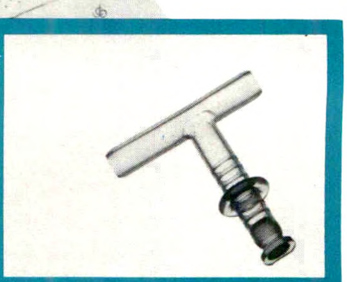

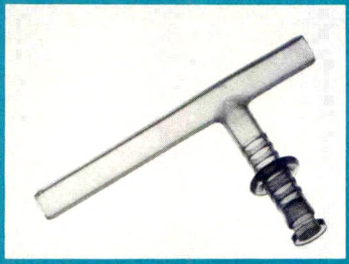

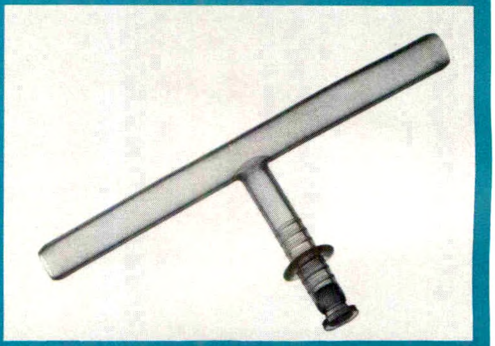

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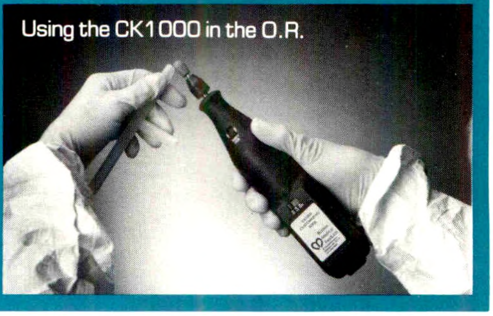

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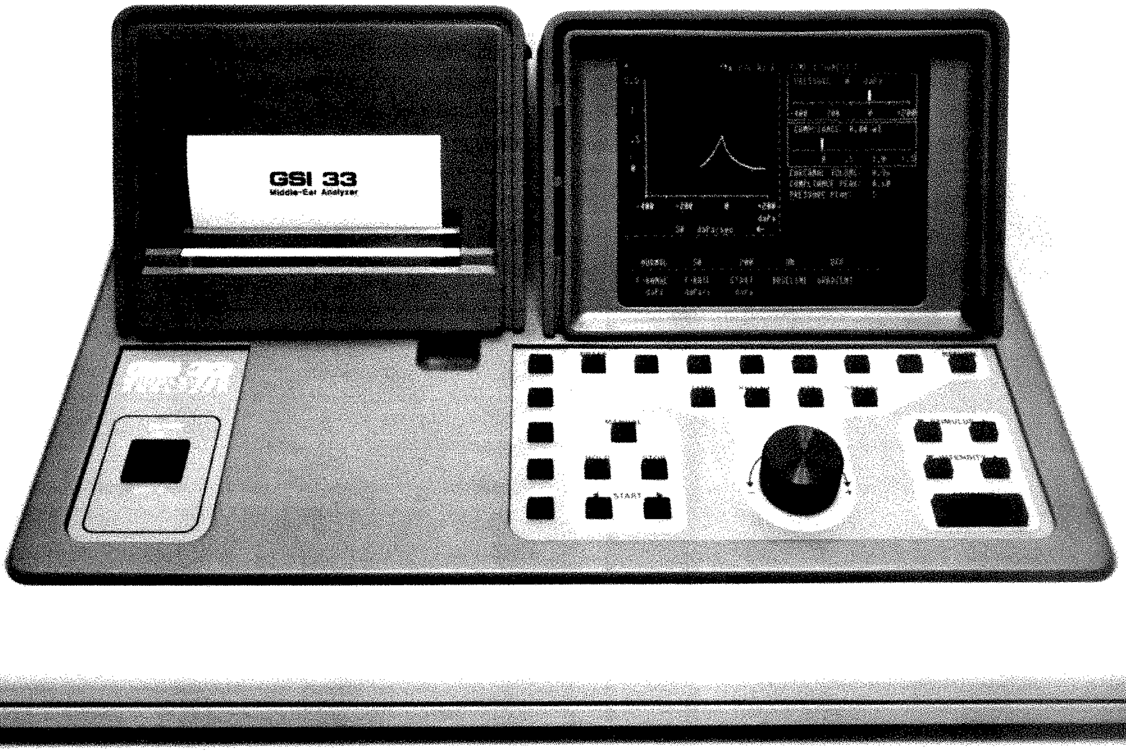

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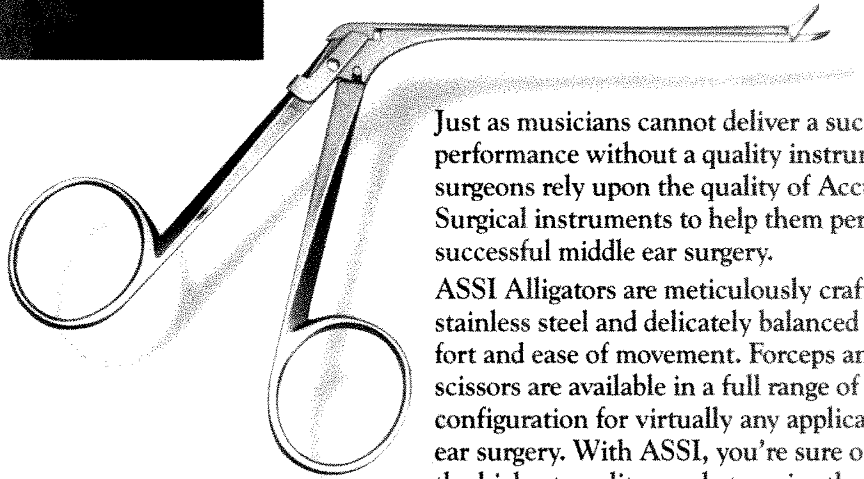

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ARYTENOID SUBLUXATION: DIAGNOSIS AND TREATMENT

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Both arytenoid subluxation and recurrent laryngeal nerve paralysis (RLNP) may result from injury to the larynx, and they may be difficult to distinguish clinically. A patient with arytenoid subluxation who was initially believed to have RLNP was treated with medialization laryngoplasty 1 year after the injury. Preoperative magnetic resonance imaging and computed tomography effectively demonstrated the cricoarytenoid subluxation, which was confirmed by intraoperative electromyography (EMG) showing normal electrical activity in the thyroarytenoid muscle. Photographs from preoperative fiberoptic laryngoscopy are presented to identify the appearance of arytenoid subluxation. Computed tomographic findings and photographs from laryngoscopy of two patients with RLNP documented by intraoperative EMG evaluation are presented to help distinguish the clinical appearance of this disorder from arytenoid subluxation. An integrated approach to the diagnosis and treatment of arytenoid subluxation is presented.

KEY WORDS — arytenoid subluxation, diagnosis, imaging, laryngeal dysfunction, laryngeal trauma.

INTRODUCTION

Laryngeal dysfunction following intubation or laryngeal trauma most often results from laryngeal edema, hemorrhage, or mucosal tears. Associated symptoms of dysphonia and sore throat are common, but are generally mild and usually resolve in 24 to 48 hours.[1,2] More significant injury may result in arytenoid subluxation or recurrent laryngeal nerve paralysis (RLNP), both of which may show an immobile lateralized vocal cord and asymmetrically positioned arytenoid cartilages upon examination with indirect laryngoscopy.[3-6] Injury as minimal as an uncomplicated intubation may cause either arytenoid subluxation by direct trauma or neuropraxia of the recurrent laryngeal nerve from pressure of the balloon cuff.[3,7-9] Differentiating between these two processes by history and physical examination may be difficult.

Arytenoid dislocation is used to describe complete separation of the arytenoid cartilage from the surface of the cricoarytenoid joint space and usually results from severe laryngeal injury. Lesser injury may result in arytenoid subluxation, which refers to abnormal displacement of an arytenoid cartilage still partially in contact with the joint space.[6]

The incidence of arytenoid subluxation or dislocation following trauma to the larynx is not known.[4,6,7] A low incidence is suggested by a prospective study of 1,000 patients in whom laryngoscopy after short-term intubation uncovered only one case of arytenoid subluxation.[10] Although only eight cases of arytenoid subluxation related to intubation injury have been reported in the English-language literature, the true incidence of this injury is suspected by some to be much higher than is generally recognized. Because of the similarity of signs and symptoms, arytenoid subluxation may be commonly misdiagnosed as RLNP.[4] The single largest series was reported in the German literature by Rudert,[11] who noted six cases of arytenoid subluxation in a series of 19 patients referred to him with laryngeal dysfunction resulting from instrumentation of the upper aerodigestive tract.

Physical findings that suggest acute arytenoid subluxation include reduced vocal cord mobility and arytenoid edema.[3] Although odynophagia has not been associated with arytenoid subluxation in all cases, it is frequently present for several days following injury and may be suggestive of subluxation rather than RLNP.[3] Long-standing cricoarytenoid subluxation with joint ankylosis may be more difficult to differentiate from RLNP once the edema and pain of the acute injury have resolved. To identify characteristics of arytenoid position that may help differentiate these processes, we employed fiberoptic videolaryngoscopy to compare the appearance of two larynges altered by RLNP with that of one with a subluxated arytenoid.

Computed tomography (CT) has been useful in identifying arytenoid subluxation and dislocation in cases in which endoscopic evaluation of the larynx is obscured by edema and hematoma or when the

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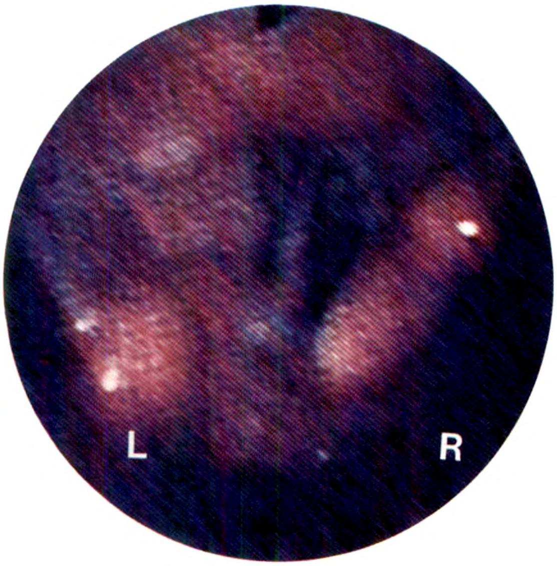

Fig 1. (Case 1) Photograph from fiberoptic videolaryngoscopy of larynx in case of right arytenoid subluxation. Asymmetry to arytenoid position is noted. Note anterior location of subluxated right arytenoid with associated bowing and lateral displacement of right vocal cord.

medical condition of the intubated patient prevents laryngoscopy.[5,12] To further define its role in imaging the injured larynx, we employed CT to evaluate the larynges of two patients in whom the distinction between arytenoid subluxation and vocal cord paralysis could not be definitively made despite adequate visualization of the larynx with fiberoptic and indirect laryngoscopy. To help determine the role of magnetic resonance imaging (MRI) in evaluating laryngeal trauma, an MRI scan was obtained as a second imaging technique in the assessment of the larynx with a subluxated arytenoid.

Although the use of electromyography (EMG) in the study of the intrinsic laryngeal muscles was first published 45 years ago, this technique has not yet found general clinical use.[13] Reports of EMG used to distinguish RLNP from arytenoid fixation have renewed interest in this application of laryngeal EMG.[6,14] We present the use of intraoperative EMG in three patients performed at the time of medialization laryngoplasty in order to help distinguish arytenoid subluxation from RLNP.

CASE REPORTS

Case 1. A 39-year-old woman incurred a neck injury in a motor vehicle accident 1 year prior to presenting at the University of Michigan otolaryngology department. She was hospitalized at the time of the accident with a normal voice and no dysphagia. Two weeks later she underwent an anterior cervical spine fusion for disc herniation and awoke from anesthesia with odynophagia and a weak voice. The hoarseness progressively worsened over the following week to the point that she could speak only in a whisper. The odynophagia persisted for only 2 days, but mild dysphagia with aspiration remained. Evaluation with indirect laryngoscopy at that time resulted in the diagnosis of right vocal cord paralysis. The patient was counseled that either laryngeal compensation or return of vocal cord mobility would likely result in resolution of the hoarseness. After 1 year of observation the hoarseness had not improved and the patient was referred to the University of Michigan.

The patient presented to the University of Michigan with a breathy voice and poor cough. Videolaryngoscopy and indirect mirror examination of the larynx revealed asymmetry of the arytenoids with anterior positioning of the right arytenoid and shortening of the right aryepiglottic fold (Fig 1). The right vocal fold was lateralized and immobile, leaving a 3- to 4-mm glottic chink upon phonation.

Computed tomography utilizing contiguous 3-mm-thick slices (General Electric, Milwaukee, Wis, CT-9800) demonstrated anteromedial displacement of the right arytenoid cartilage as seen on direct axial images and on reformatted sagittal and coronal images (Fig 2). There was paramedian positioning of the right true vocal fold and enlargement of the right laryngeal ventricle. Sequential images at more rostral levels demonstrated thickening of the right aryepiglottic fold and mild prominence in size of the right pyriform sinus.

Magnetic resonance imaging (General Electric, Milwaukee, Wis, 1.5T Signa) was completed with a prototype laryngeal surface coil with T1 contrast-weighted images (TR 500/TE 20 milliseconds, 128 x 256 matrix, 3-mm or 4-mm slice thickness, 2 or 4 excitations, 20-cm field of view) employed to best image the laryngeal framework. The right arytenoid cartilage as imaged on sagittal, coronal, and axial orientation was clearly seen to be anteriorly displaced relative to the cricoid cartilage (Fig 3).

A laryngeal framework operation with vocal cord medialization was performed under local anesthesia. Prior to manipulating the right vocal cord, monopolar hooked wire electrodes were placed into the left thyroarytenoid muscle through the cricothyroid membrane and into the right thyroarytenoid muscle through the window created in the right thyroid lamina (Fig 4). Correct placement of the electrodes was determined by inspection with transnasal fiberoptic laryngoscopy. A reference electrode was placed in the left arm. Symmetric muscle action potential patterns were separately recorded with monopolar electrodes from both vocalis muscles upon phonation (Fig 5). To more accurately localize the recorded electrical activity to the thyroarytenoid muscle, the monopolar electrodes were removed and a bipolar hooked wire electrode with an intertip distance of less than 1 mm was placed through the window in the right thyroid lamina into the thyroarytenoid muscle. Phonation consistently produced clearly defined muscle action potential

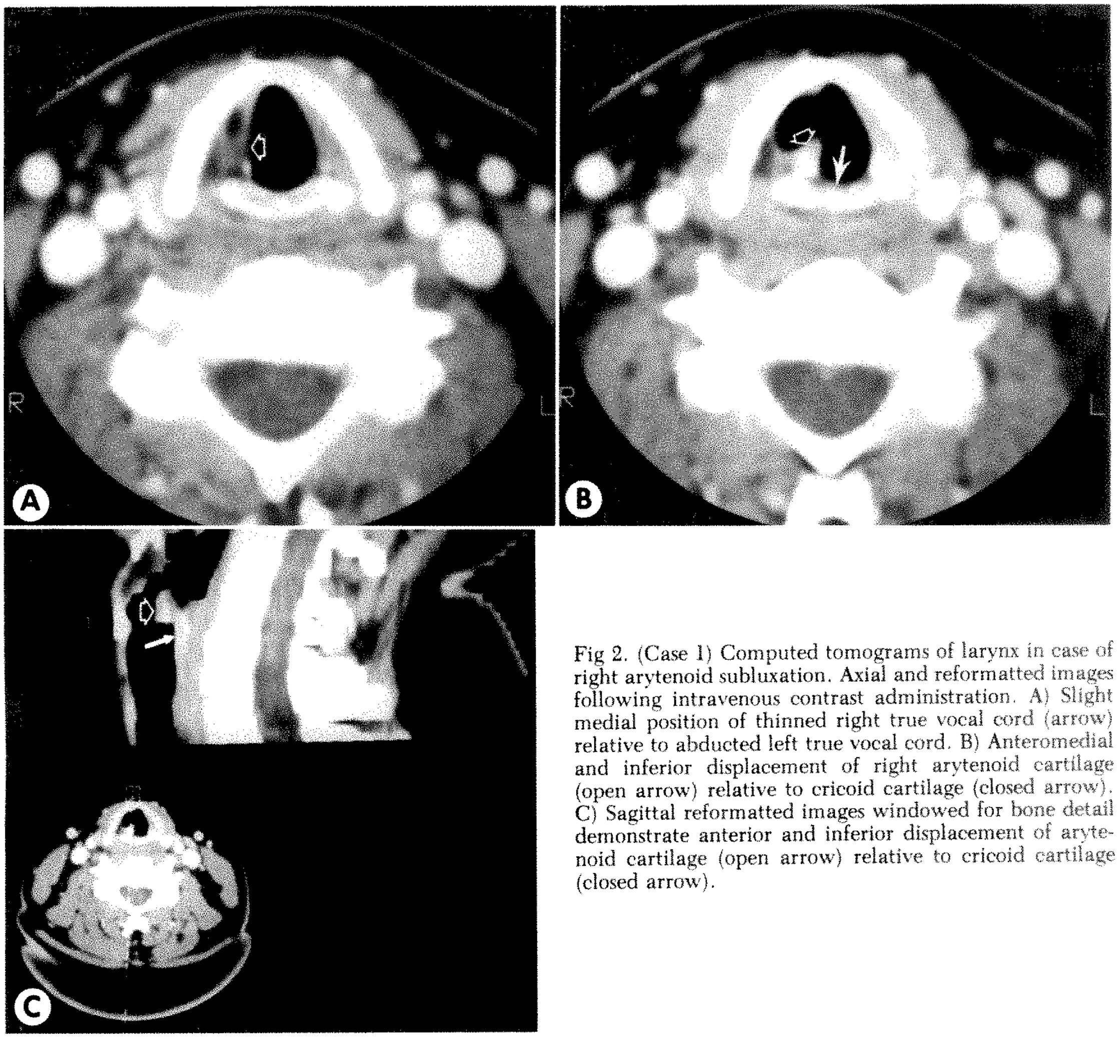

Fig 2. (Case 1) Computed tomograms of larynx in case of right arytenoid subluxation. Axial and reformatted images following intravenous contrast administration. A) Slight medial position of thinned right true vocal cord (arrow) relative to abducted left true vocal cord. B) Anteromedial and inferior displacement of right arytenoid cartilage (open arrow) relative to cricoid cartilage (closed arrow). C) Sagittal reformatted images windowed for bone detail demonstrate anterior and inferior displacement of arytenoid cartilage (open arrow) relative to cricoid cartilage (closed arrow).

trains from the thyroarytenoid muscle that were not present during quiet respiration (Fig 6).

The bipolar electrodes were removed and the right vocal cord, thyroarytenoid muscle, and underlying thyroid cartilage segment were medialized to an optimal location as determined by voice assessment and inspection with the fiberoptic laryngoscope. The medialized complex was then secured with a sculpted segment of Silastic with modifications in the technique previously described.[15-18] Eleven days following the procedure, videolaryngoscopy demonstrated a medialized vocal fold with much improved glottic closure.

Case 2. A 38-year-old woman required intubation and gastric lavage with a Ewald tube in the emergent treatment of a drug overdose at an outside hospital. She was noted to be hoarse upon extubation and developed a left upper lobe pneumonia and lung abscess resulting from an esophageal perforation thought to have occurred at the time of resuscitation. She was transferred to the University of Michigan, where she was treated with drainage of the left thorax through a combined left cervical and posterior thoracic approach. The patient recovered without long-term sequelae other than persistent hoarseness that prompted a referral to the otolaryngology department 8 months later.

Indirect mirror examination and videolaryngoscopy at that time revealed an anteriorly positioned, immobile left arytenoid with a lateralized left true vocal cord (Fig 7). The left aryepiglottic fold was shortened and a 3- to 4-mm glottic chink was present on attempted phonation.

Computed tomography (GE CT-9800) demonstrated asymmetric positioning of the vocal cords with thinning of the left vocal cord (Fig 8). The arytenoid cartilage was positioned normally in relation to the cricoid cartilage.

Nine months following the initial injury, the patient was treated with medialization laryngoplasty, at which time bipolar hooked wire electrodes were placed into the left thyroarytenoid muscle. Figure 9 illustrates the EMG activity recorded during quiet respiration (upper trace) and phonation (lower trace). The difference between these two conditions is minimal; this finding confirms a diagnosis of severely compromised innervation of the left thyroarytenoid muscle.

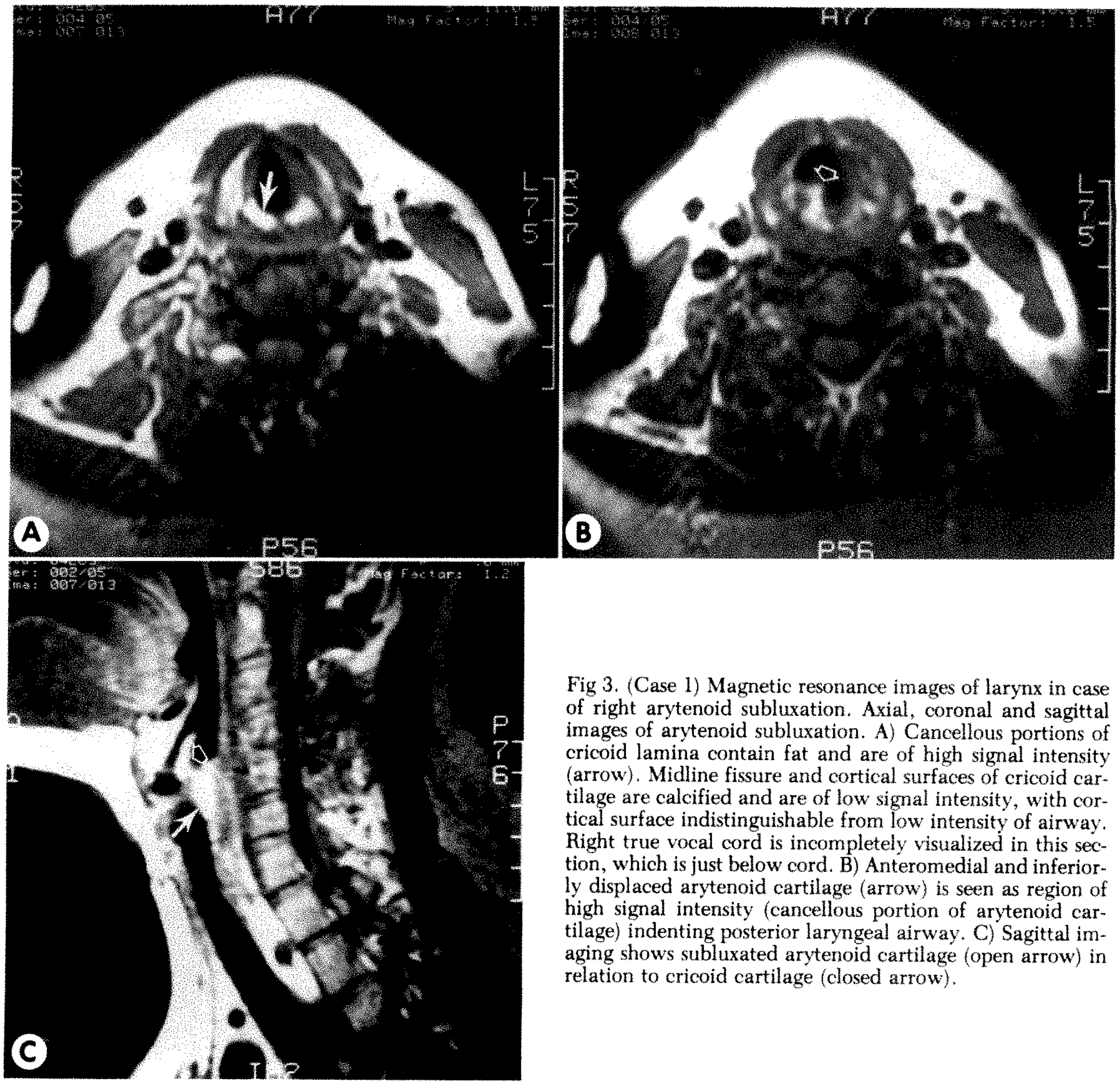

Fig 3. (Case 1) Magnetic resonance images of larynx in case of right arytenoid subluxation. Axial, coronal and sagittal images of arytenoid subluxation. A) Cancellous portions of cricoid lamina contain fat and are of high signal intensity (arrow). Midline fissure and cortical surfaces of cricoid cartilage are calcified and are of low signal intensity, with cortical surface indistinguishable from low intensity of airway. Right true vocal cord is incompletely visualized in this section, which is just below cord. B) Anteromedial and inferiorly displaced arytenoid cartilage (arrow) is seen as region of high signal intensity (cancellous portion of arytenoid cartilage) indenting posterior laryngeal airway. C) Sagittal imaging shows subluxated arytenoid cartilage (open arrow) in relation to cricoid cartilage (closed arrow).

Case 3. A 43-year-old woman was referred to the University of Michigan with a feeling of fullness in the right side of the neck and the observation of swelling in the right posterior pharyngeal wall. A right parapharyngeal space mass was identified on CT scan and subsequently excised through a cervical approach. Resection of the tumor, determined to be a schwannoma on histopathologic evaluation, required sacrifice of a segment of the vagus nerve, from which it was emanating.

Postoperatively the patient noted dysphagia with aspiration and a weak voice that persisted despite speech therapy. Four months after resection of the tumor, videolaryngoscopy was performed, demonstrating an asymmetric appearance to the arytenoids with lateralization of the right vocal cord and an approximately 3-mm gap between the vocal cords upon attempted phonation (Fig 10).

Medialization laryngoplasty was performed with intraoperative EMG evaluation of recurrent laryngeal nerve function. Bipolar hooked wire electrodes were placed into both thyroarytenoid muscles. Recording from the right thyroarytenoid muscle (top two traces, Fig 11) resulted in complete electrical silence during both quiet respiration and phonation. In contrast, reduced background EMG activity during respiration and significant activation during phonation are evident on the left side (bottom two traces, Fig 11).

DISCUSSION

The biomechanics of arytenoid displacement resulting in subluxation have not been definitively identified, although many mechanisms have been postulated. Most reports of arytenoid subluxation following intubation describe anterior positioning of the displaced arytenoid.[4-6,8,19] Forces applied directly to the arytenoid in a posterior-to-anterior direction from an endotracheal tube or laryngoscope blade have been listed among the causes for such displacement. The presence of a normally strong posterior cricoarytenoid ligament that would resist anterior displacement of the arytenoid cartilage has

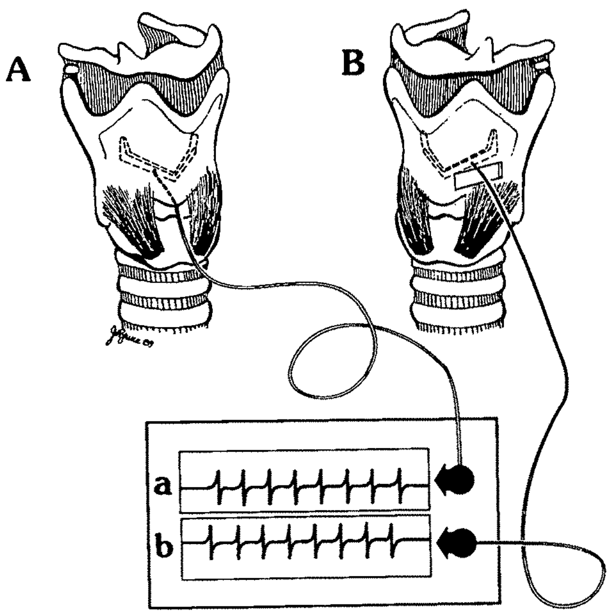

Fig 4. Diagram showing placement of electrodes from electromyographic monitoring of thyroarytenoid muscle function intraoperatively. External approach to vocal cord medialization under local anesthesia offers direct access for evaluation of neuromuscular function of intrinsic laryngeal musculature. Bipolar hooked wire electrodes are placed into thyroarytenoid muscles either (A-a) through cricothyroid membrane (on normal side) or (B-b) through window in thyroid cartilage adjacent to lateralized cord.

made some investigators skeptical of the potential for arytenoid subluxation occurring in a normal larynx without trauma significant enough to disrupt this ligament[20] (also N. Olson, personal communication, 1989). Previously reported cases of arytenoid subluxation have listed associated abnormalities including laryngomalacia, acromegaly, and chronic steroid use that may have contributed to either weakening of the posterior ligament or degeneration of the cricoarytenoid joint and predisposition to subluxation.[2-4,19] However, no anatomic abnormality or disease process has been consistently associated with arytenoid subluxation.

Posterior subluxation of the arytenoid cartilage has also been described.[11,21] Posterior displacement has been attributed to a posterolateral force applied to the arytenoid from the convex curvature of the distal third of the endotracheal tube as it is inserted.[3] The stretching of the aryepiglottic fold that occurs upon elevation of the supraglottis with insertion of the direct laryngoscope has been proposed as a maneuver that may compromise the stability of the joint and predispose it to subluxation.[3] It has also been proposed that posterior subluxation may result from trauma to the arytenoid by withdrawal of an endotracheal tube with a balloon that is only partially deflated.[5,6]

Arytenoid dislocation from external neck trauma is often accompanied by other laryngeal injuries.[12] Stanley and Colman[22] described three such cases of arytenoid cartilage dislocation, accompanied by overlying mucosal tears, that resulted in an anteromedial positioning of the arytenoid. Blunt injury to the neck may subluxate the arytenoid by lateral pressure of the medially displaced thyroid ala on the arytenoid.[22] Other authors have suggested that posterior displacement of the arytenoid cartilages may result from trauma directed to the anterior thyroid cartilage that causes the splayed thyroid ala to push the arytenoid backward.[23,24]

The cause of arytenoid subluxation is not clear in the first case presented. Although the patient did receive a neck injury of sufficient degree to cause a cervical spine fracture, hoarseness did not develop until after an anterior cervical spine fusion was performed. Intubation injury or trauma to the larynx at the time of operation could have caused the arytenoid subluxation.

Prior to the availability of CT, direct laryngoscopy was required to substantiate the diagnosis of arytenoid subluxation. Palpation of the arytenoid at the time of endoscopy with closed reduction of an abnormally positioned arytenoid has been the definitive diagnostic procedure used to confirm arytenoid cartilage subluxation.[25] This evaluation, however, may be misleading if the arytenoid cartilage becomes fixed in an asymmetric position from a process other than subluxation. Cricoarytenoid arthritis from systemic autoimmune disease or adjacent infection may result in joint ankylosis. Longstanding vocal cord paralysis may also result in fibrosis of the cricoarytenoid joint.[23,26] Palpation of the fixed arytenoid at the time of direct laryngoscopy in these cases would possibly result in the misdiagnosis of arytenoid subluxation with ankylosis.

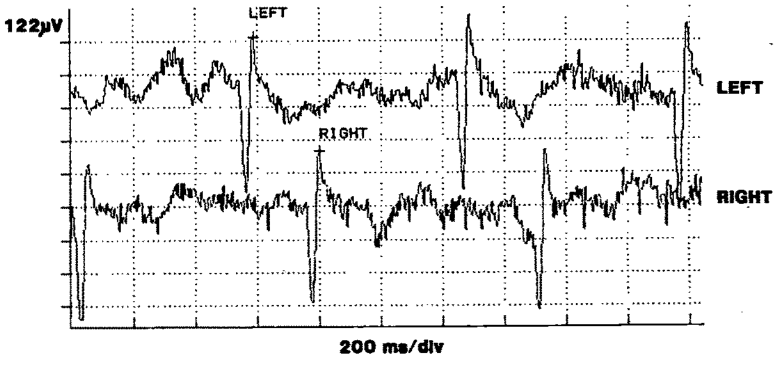

Fig 5. (Case 1) Electromyographic recordings (monopolar) of thyroarytenoid muscle function in case of right arytenoid subluxation. Unipolar recordings comparing electrical activity in right and left thyroarytenoid muscle function were obtained during medialization laryngoplasty for right arytenoid subluxation. Action potentials of equal amplitude and frequency are recorded from both sides during phonation.

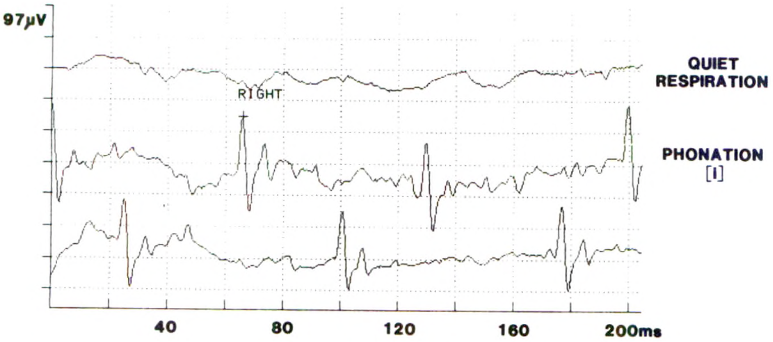

Fig 6. (Case 1) Electromyographic recordings (bipolar) of thyroarytenoid muscle function in case of right arytenoid subluxation. Bipolar hooked wire electrodes were placed in right thyroarytenoid muscle. Presence of normal motor unit action potentials generated during phonation indicates normal innervation.

As more experience with advanced imaging techniques is acquired, CT is likely to be found more reliable than direct laryngoscopy in documenting arytenoid subluxation. From an anatomic study of 20 adult larynges, Maue and Dickson[20] discovered consistent symmetry between the arytenoid cartilages and the cricoarytenoid facets, which were "well defined, very consistent, and bilaterally symmetric in all cases." Disruption in this symmetry between arytenoids and an altered cricoarytenoid relationship is clearly revealed by CT.[27]

The CT alterations associated with arytenoid subluxation have been described in two previous patients.[5,6] In both cases the body of the arytenoid cartilage was anteromedially and inferiorly displaced, with the superior process of the arytenoid displaced posteriorly in one of the cases. The radiographic images of the subluxated arytenoid we report show a similar anteromedial and inferior displacement of the arytenoid body, but without posterior displacement of the superior process.

The CT imaging characteristics of RLNP have been well described[28,29] and share several common features with arytenoid subluxation. Both laryngoscopy and CT imaging frequently show a paralyzed vocal cord to be lateralized with an accompanying altered angulation of the aryepiglottic fold and enlargement of the ventricle. The abnormal positioning of the supraglottic structures as noted upon fiberoptic laryngoscopy of the larynx with left vocal cord paralysis (case 2) resulted from displacement of the soft tissue overlying a normally positioned arytenoid cartilage as shown on CT (Figs 7 and 8). Although paralysis of the adjacent muscular attachments may allow a slight anteromedial rotation and anteromedial displacement of the arytenoid cartilage relative to the cricoid cartilage in patients with RLNP, this displacement is minimal and is clearly distinguished from arytenoid subluxation in the cases presented as well as in previously published reports. As a result, we conclude that the imaging parameter that best distinguishes arytenoid subluxation from RLNP is the relationship of the arytenoid to the cricoid cartilage.

Magnetic resonance imaging of arytenoid subluxation has not previously been reported. Magnetic resonance and CT imaging proved to be equally efficacious in documenting arytenoid subluxation and in demonstrating the degree of laryngeal disruption in the case presented. Magnetic resonance imaging offers the advantages of allowing direct sagittal imaging without relying on reformatting of axial images while sparing the patient exposure to ionizing radiation. It is evident, however, that the cortical margins of the laryngeal cartilages are better visualized with CT than with MRI techniques. Although MRI is generally superior to CT for imaging the interface between soft tissues, CT imaging may continue to be preferred in situations that require identification of the relationship between adjacent cartilaginous or calcified structures. For these reasons as well as problems with cost, lack of general availability, and difficulty with motion artifact seen with MRI, CT imaging at present remains our preferred method of imaging arytenoid subluxation.

Our study provides the second reported case in which CT has been used to differentiate arytenoid subluxation from vocal cord paralysis in a larynx

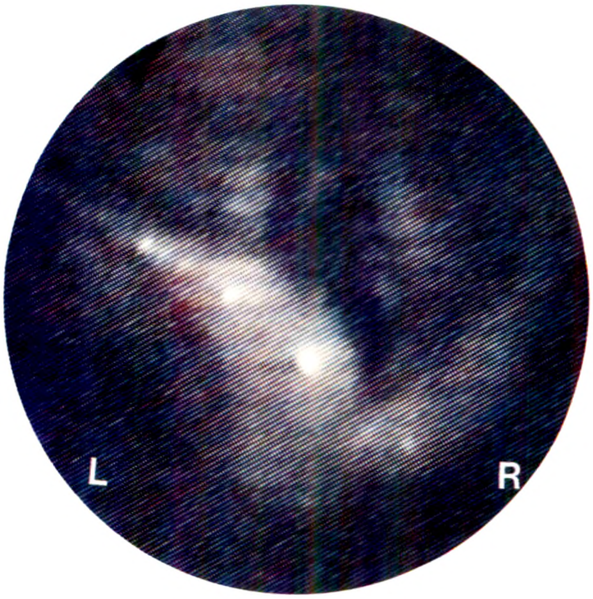

Fig 7. (Case 2) Photograph from fiberoptic videolaryngoscopy of larynx in case of left recurrent nerve paralysis. Anteriorly positioned, immobile left arytenoid with shortened and angulated left aryepiglottic fold is noted. Dynamic videolaryngoscopy revealed immobile left vocal cord in lateral position, leaving 4-mm glottic chink upon attempted phonation.

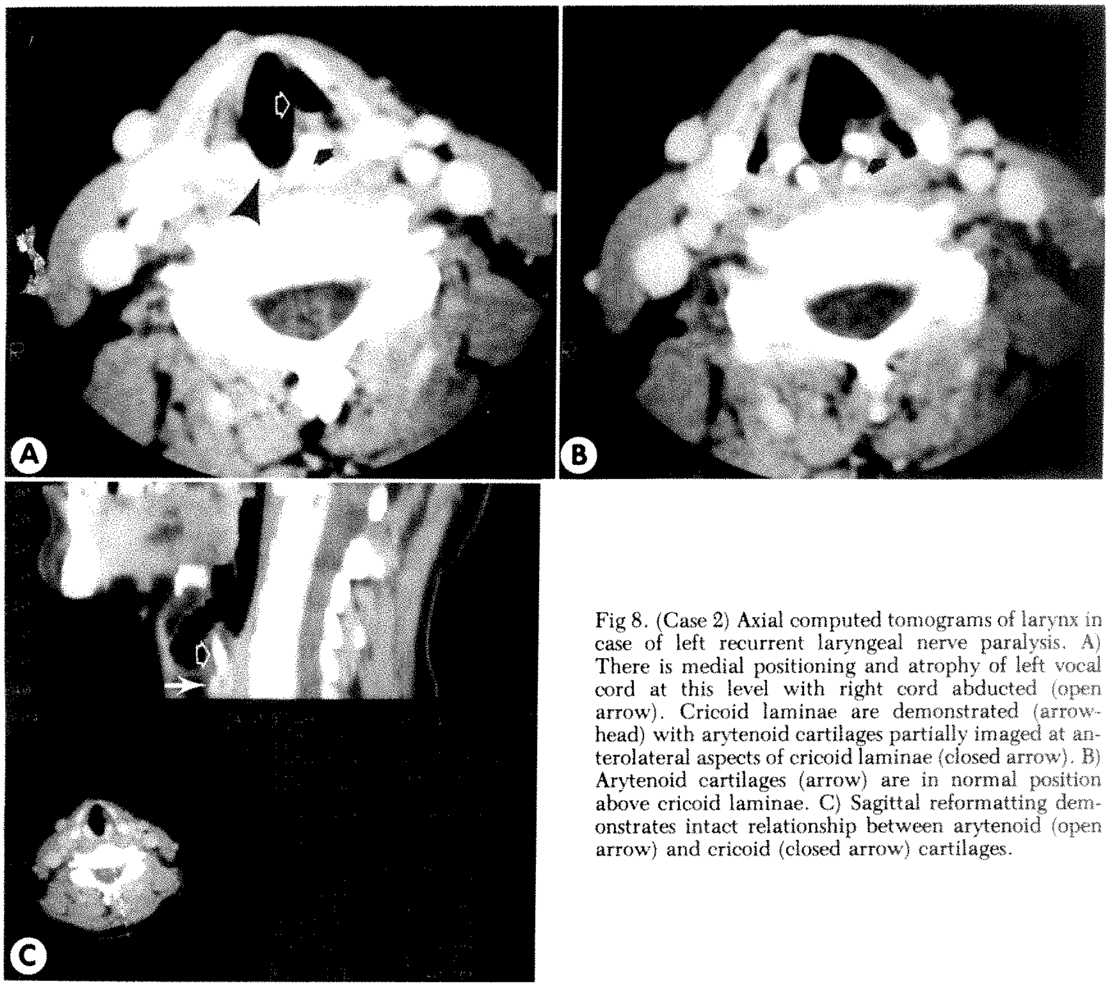

Fig 8. (Case 2) Axial computed tomograms of larynx in case of left recurrent laryngeal nerve paralysis. A) There is medial positioning and atrophy of left vocal cord at this level with right cord abducted (open arrow). Cricoid laminae are demonstrated (arrowhead) with arytenoid cartilages partially imaged at anterolateral aspects of cricoid laminae (closed arrow). B) Arytenoid cartilages (arrow) are in normal position above cricoid laminae. C) Sagittal reformatting demonstrates intact relationship between arytenoid (open arrow) and cricoid (closed arrow) cartilages.

that is well visualized.[5] It is important to distinguish between these two processes in order that closed reduction of a subluxated arytenoid be performed before irreversible joint fixation occurs. Conversely, the diagnosis of vocal cord paralysis as supported by CT demonstrating a normally positioned arytenoid would spare the patient the need for a direct laryngoscopy to rule out arytenoid dislocation.

Intraoperative EMG monitoring of laryngeal neuromuscular activity employing the technique we describe has not been previously reported. In the three cases presented, EMG was used to confirm a diagnosis obtained from clinical evaluation and imaging studies. Electromyography may also be used preoperatively to help in treatment planning. Although the accurate placement of electrodes is more difficult when done percutaneously than when done through the open approach we describe, laryngeal EMG may be performed as a clinic procedure.[14] Information regarding both superior laryngeal nerve function and recurrent laryngeal nerve function may be obtained by this test.

Restoration of normal anatomic relationships in the injured larynx is generally thought to provide the best functional result. However, reduction of a displaced arytenoid may not restore vocal cord mobility and normal laryngeal function.[6,11,25,30] Arytenoid cartilage fixation has been reported to occur as early as 24 to 48 hours following subluxation.[6,23] After this time, even successful anatomic reduction of the displaced arytenoid may result in laryngeal dysfunction due to limitation of arytenoid mobility.[8,11,22,25] We feel it is best to treat arytenoid sub-

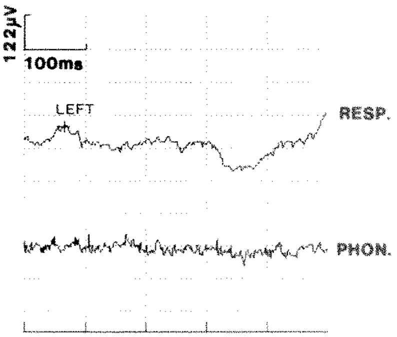

Fig 9. (Case 2) Electromyographic recordings (bipolar) of thyroarytenoid muscle function in case of left recurrent laryngeal nerve paralysis. Bipolar hooked wire electrodes were placed through window created in thyroid cartilage adjacent to immobile vocal cord. Although some minimal background electrical activity was noted during both quiet respiration and phonation, difference between these two conditions is minimal, confirming diagnosis of severely compromised innervation of left thyroarytenoid muscle.

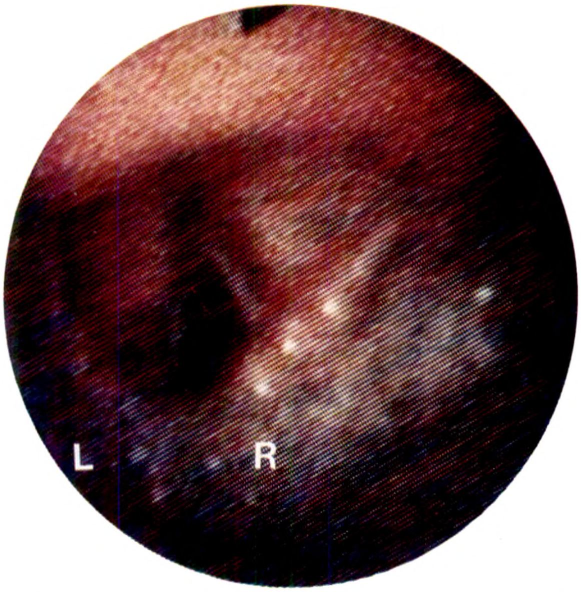

Fig 10. (Case 3) Photograph from videolaryngoscopy of larynx with right recurrent laryngeal nerve paralysis. Asymmetry of arytenoid is noted upon inspiration, with right arytenoid and aryepiglottic fold anteriorly displaced and angulated relative to left. Right vocal cord is bowed and laterally placed, leaving 3-mm glottic chink upon attempted phonation.

luxations with attempted reduction if the disorder is identified within 1 month of the onset of symptoms. Failure to restore normal laryngeal function following reduction of the subluxated arytenoid cartilage may then be followed by vocal cord medialization with a laryngeal framework procedure.

This report is the first of the use of a laryngeal framework procedure as adapted from Isshiki et al[15-17] and Kaufman[18] to treat arytenoid subluxation. We employ this technique as the initial treatment for arytenoid subluxation only when we feel there is no chance for return of normal arytenoid mobility with closed reduction. Treatment in these instances may be performed without direct laryngoscopy when the diagnosis is established radiographically.

Other methods for treatment of arytenoid subluxation have been described and include Teflon injection and cricoarytenoid arthrodesis.[19] The Montgomery arthrodesis technique involves reduction with pin fixation of a lateralized arytenoid via a laryngofissure.[26] This technique suffers from the need for a tracheostomy, general anesthesia, and a more extensive procedure that has the potential to injure other regions of the larynx. Teflon injection is a time-honored method of medializing a lateralized vocal cord that can be done under local anesthesia in an expeditious manner. Disadvantages of Teflon injection include the potential for migration of the Teflon, alteration of the characteristics of the free vibrating segment of the vocal cord, patient discomfort from direct laryngoscopy performed under local anesthesia, and difficulty in accurate placement of the Teflon. Adequate treatment of glottic insufficiency due to arytenoid subluxation may be difficult with Teflon injection because of the lateral position the vocal cord generally assumes. The treatment of arytenoid subluxation with vocal cord medialization via a laryngeal framework procedure permits an aggressive advancement of a lateralized cord without disturbing the characteristics of the free edge of the cord. For these reasons, and the ability to perform the procedure without patient discomfort under local anesthesia, we prefer medialization laryngoplasty over Teflon injection for the treatment of arytenoid subluxation.

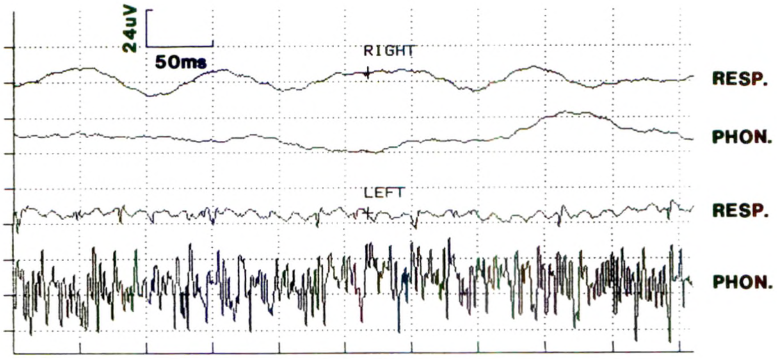

Fig 11. (Case 3) Electromyographic recording (bipolar) of thyroarytenoid muscle function in case of right recurrent laryngeal nerve paralysis. Simultaneous recordings were obtained from hooked wire bipolar electrodes placed into right and left thyroarytenoid muscles at time of medialization laryngoplasty. Note complete lack of electrical activity in right thyroarytenoid muscle during both respiration and attempted phonation.

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Ann Otol Rhinol Laryngol 100:1991

RECURRENT LARYNGEAL NERVE AVULSION FOR TREATMENT OF SPASTIC DYSPHONIA

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Treatment of spastic dysphonia by recurrent laryngeal nerve section has resulted in reproducibly good results in the early postoperative period in most patients. However, critical long-term follow-up has shown a high recurrence rate of adductor spasms by the third year after initial nerve section. A patient who developed recurring adductor spasms 1 year after nerve section was reexplored, with identification of neural regrowth into the distal segment of the recurrent laryngeal nerve. The technique of neural avulsion removing the distal nerve up to its insertion into the laryngeal muscles is described. Neural regrowth, which is just one of the possible mechanisms for recurrence of spastic dysphonia, should be prevented by this surgical modification. Twelve patients who have undergone neural avulsion primarily for spastic dysphonia are being followed up without recurrence of symptoms thus far. Although these results appear promising, this short follow-up that averages 1.5 years must be extended to firmly support these concepts.

KEY WORDS — recurrent laryngeal nerve avulsion, recurrent laryngeal nerve section, spastic dysphonia.

INTRODUCTION

Recurrent laryngeal nerve section for treatment of spastic dysphonia, introduced in 1976 by Dedo,[1] appeared to be the first reliable treatment for the many patients whose lives were severely altered by this disease. This procedure, however, became shadowed by a cloud of doubt due to the significant recurrence rate of the adductor spasms within the first 3 years after operation. Many mechanisms of the cause of this recurrence have been postulated, but few proved. Regrowth of the recurrent laryngeal nerve, which was first implied by Wilson et al,[2] has not been included as a reasonable cause of recurrence by most authors. Through the presentation of our patient, who underwent a revision operation for recurrence of spastic dysphonia 2 years after recurrent laryngeal nerve section, and a review of the literature, we would like to emphasize two points. One is that neural regrowth into the distal stump of the recurrent laryngeal nerve, whether from the proximal cut end of the recurrent laryngeal nerve or sprouting from other motor nerves in the region, is one mode of recurrence of spastic dysphonia. The other is that neural avulsion rather than nerve section is a surgical modification that should prevent this mechanism of failure.

CASE REPORT

A 50-year-old woman first presented with the onset of spastic dysphonia in 1976 at the age of 36. Over the next 8 years, she underwent treatment by all of the nonoperative modalities available, including a 3-month stay in a psychiatric hospital for evaluation and treatment. No lasting improvement was noted in her adductor spasms with any of these treatments.

In 1986, she underwent a left recurrent laryngeal nerve section removing 1.5 cm of the nerve inferior to the lower thyroid border. This resulted in initial excellent vocal improvement, with a slightly breathy voice free of adductor spasms. A good-quality voice was sustained for 12 months, and then symptoms of spastic dysphonia recurred. She first presented to our institution in early 1988 for evaluation. Examination demonstrated classic adductor spastic dysphonia. Video laryngoscopy revealed a complete paralysis of the left true vocal cord with hyperfunction of the right hemilarynx. No mucosal wave was demonstrated on the left vocal cord with stroboscopic examination. The patient underwent injection of 5 mL of 1% lidocaine in the region of the left recurrent laryngeal nerve just inferior to the lower border of the thyroid gland, which resulted in marked reduction of the adductor spasms. She was subsequently taken to the operating room and explored through her previous incision. The distal stump of the recurrent laryngeal nerve was identified deep to the mobilized left thyroid lobe. The nerve was followed to its passage under the cricopharyngeus and avulsed from its insertions into the laryngeal musculature. Postoperatively, her voice returned to the same good quality as after her first nerve section. The proximal end of this avulsed segment was closely examined histologically, and neural regeneration into the nerve stump was noted (see Figure, A). She has maintained this improved voice quality for 2 years postoperatively.

DISCUSSION

Spastic dysphonia is a poorly understood altera-

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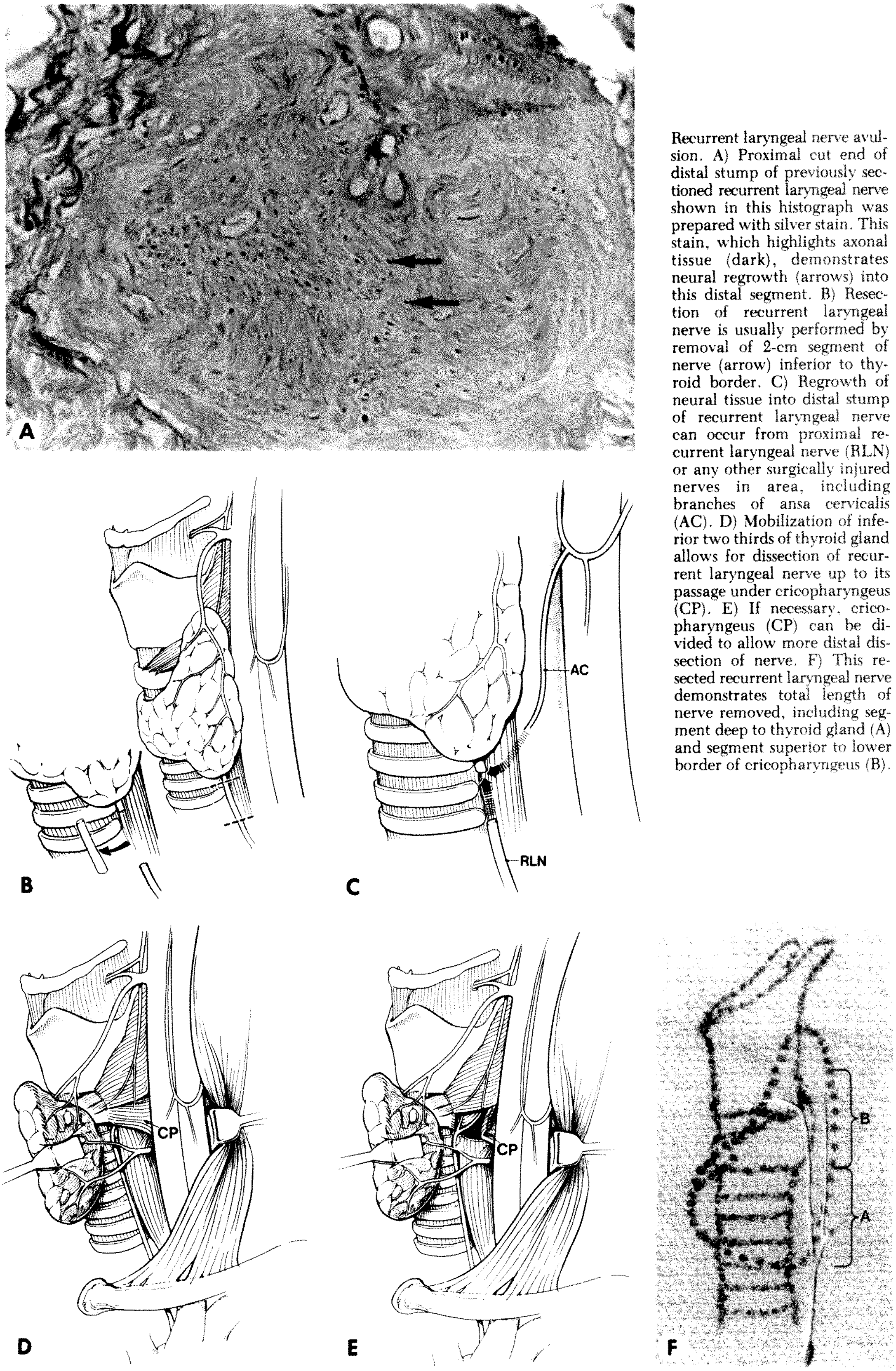

Recurrent laryngeal nerve avulsion. A) Proximal cut end of distal stump of previously sectioned recurrent laryngeal nerve shown in this histograph was prepared with silver stain. This stain, which highlights axonal tissue (dark), demonstrates neural regrowth (arrows) into this distal segment. B) Resection of recurrent laryngeal nerve is usually performed by removal of 2-cm segment of nerve (arrow) inferior to thyroid border. C) Regrowth of neural tissue into distal stump of recurrent laryngeal nerve can occur from proximal recurrent laryngeal nerve (RLN) or any other surgically injured nerves in area, including branches of ansa cervicalis (AC). D) Mobilization of inferior two thirds of thyroid gland allows for dissection of recurrent laryngeal nerve up to its passage under cricopharyngeus (CP). E) If necessary, cricopharyngeus (CP) can be divided to allow more distal dissection of nerve. F) This resected recurrent laryngeal nerve demonstrates total length of nerve removed, including segment deep to thyroid gland (A) and segment superior to lower border of cricopharyngeus (B).

tion from normal laryngeal function. For almost a century after Traube's[3] description of this disorder in 1871, it was considered a functional or "hysterical" disease resulting from stress or other emotional problems. This theory resulted in a variety of ineffective treatments aimed at treating the underlying emotional disorder. Although the probable organic nature of this disease is now widely accepted, nonoperative treatments are still usually ineffective. Voice therapy including relaxation therapy has been extensively used in the treatment of these patients, with only modest success.

The initial description of recurrent laryngeal nerve section in 1976 by Dedo[1] seemed to hold promise as the first dependable treatment for this disorder. In his first series of 34 patients treated with nerve resection followed by voice therapy, near-normal voice quality was achieved in half the patients. The remainder were "pleased" with relative voice improvement and the marked ease of communication with little vocal effort. Barton[4] in 1979 reported initial satisfactory results in 8 of 11 patients, while the other 3 received moderate benefit from the recurrent laryngeal nerve section. The follow-up of both of the above reports, however, was relatively short.

Levine et al[5] reported on 22 patients followed up from 6 to 36 months after operation who underwent sectioning of the recurrent laryngeal nerve. In this group, 17 sustained a good result, while 5 patients ultimately developed some recurrence of laryngeal spasm. Aronson and DeSanto[6] in 1981 presented 37 patients who had undergone nerve section for spastic dysphonia. They found a slow increase in recurrence rate — 8% at 6 months, 32% at 1 year, and 39% at 1½ years — and advised long-term follow-up to truly test the efficacy of nerve section as a treatment for spastic dysphonia. Dedo and Izdebski[7] updated the Dedo series in 1983, noting that 80% of 306 patients who had undergone recurrent laryngeal nerve section "gave unqualified recommendation for this procedure." Only 5.5% reported no difference, and 2.5% felt communication was more difficult after the operation. Aronson and DeSanto[8] in 1983 updated their series with a 3-year follow-up on 33 of the patients who had undergone nerve section. Although only 18% had return of symptoms at 1 year, by the second- and third-year marks 42% and 64%, respectively, failed with return of adductor spasms. This report, which questioned the validity of nerve section as a treatment for spastic dysphonia, resulted in a marked decrease in the use of this procedure in the following years. Aronson and DeSanto felt that failure was not due to reinnervation of the paralyzed true vocal cord, in that no return of motion in the paralyzed vocal cord was noted in any of the patients with documented recurrence. They felt the cause of recurrence was secondary to hyperadduction of the normal true vocal cord and the sphincteric action of the false vocal folds.

These findings sparked an ongoing debate as to the cause of recurrence of spastic dysphonia after recurrent laryngeal nerve section. The more popular theories include straining, hyperadduction, sphincteric action of the false vocal folds, and progression of the initial "neurologic disorder." Neural regrowth has not been widely accepted as a viable option by most authors. Possible regrowth of the recurrent laryngeal nerve was first reported by Wilson et al[2] in 1980. This report centered on a patient who redeveloped spastic dysphonia 9 months after resection of a 1-cm segment of the right recurrent laryngeal nerve. Upon reexploration 13 months after the initial nerve section, the nerve was found to be intact and thus was re-resected with resolution of the adductor spasms postoperatively. A careful examination of this paper might lead one to believe that the nerve was damaged but not sectioned during the first procedure. The excellent report by Schiratzki and Fritzell[9] in 1988 is more convincing, however. In this report, 4 of 12 patients who had undergone recurrent laryngeal nerve section removing 2 cm of the infrathyroid nerve developed recurrence 4 to 10 months after the initial nerve resection. Two of these patients who were early in the series were reexplored to rule out regrowth of neural tissue. The distal stump of the recurrent laryngeal nerve was not found in either patient, but 1 of the 2 patients obtained marked vocal improvement from the dissection only. This was probably secondary to disruption of the delicate neural fibers that occur with neural regrowth. In the second group of 2 patients who were reexplored for recurring symptoms, the distal cut end of the recurrent laryngeal nerve had been ligated with silver clips during the original operation secondary to the earlier failures described above. Upon reexploration of each of these two patients, the distal stump of the nerve, with the silver clip, was identified and further resected, resulting in resolution of the adductor spasms postoperatively in both patients.

Examination of the operative description in each of the large series described above shows that the length of nerve resected ranged from 1 to 3.5 cm, with an average of 2 cm. This resection was routinely performed in the infrathyroid portion of the nerve (see Figure, B). One can logically assume from the above cases that resection of a segment of the recurrent laryngeal nerve leaving an open distal stump can allow for regrowth of neural tissue into this nerve segment. This regrowth may occur from the proximal recurrent laryngeal nerve stump or any other regional motor nerve such as a branch of the ansa cervicalis that was divided during the original nerve section (see Figure, C). This reinnervation does not usually lead to reanimation with movement of the vocal cord, but does provide static muscular tone leading to recurring adductor spasms.

It is uncertain whether regrowth into this distal segment by a regional sensory or autonomic nerve could develop enough resting tone in the paralyzed larynx to cause recurrence of spasms.

Dedo[10] attributes his low occurrence rate to silk ligatures placed on the cut nerve ends at the time of resection. This indeed may help to detour neural regrowth, but the report by Shiratzki and Fritzell,[9] as well as data derived by Crumley and McCabe[11] demonstrating neural regrowth over a 2.5-cm segment into the tightly suture-ligated distal stump of the recurrent laryngeal nerve implies that ligation is not a dependable method to prevent neural regrowth.

Early analysis of these data led us to modify recurrent laryngeal nerve section into neural avulsion of the entire distal nerve in an attempt to prevent this regrowth. This is performed through the same exposure as recurrent laryngeal nerve section. One modification of the original procedure includes mobilization of the thyroid and dissection of the recurrent laryngeal nerve close to its insertion into the laryngeal musculature (see Figure, D). The recurrent laryngeal nerve is first identified inferior to the thyroid gland and is then dissected superiorly, with the surgeon carefully identifying and following each of the early branches of the nerve. We have seen the nerve give off as many as six branches prior to passing under the cricopharyngeus muscle. Each of these branches is followed as distally as possible. With two DeBakey forceps, these nerves are grasped, the forceps are slowly walked forward, and the nerve is avulsed from its distal insertion. We routinely remove 3 cm of nerve beyond its passage under the cricopharyngeus. When it appears that the nerve might be quite delicate and separate early, the cricopharyngeus muscle is mobilized to allow a more distal dissection of the nerve (see Figure, E). After the entire distal insertion of the nerve has been avulsed, the nerve is followed under the clavicle for 3 to 4 cm more. With tension on the nerve, the proximal segment is ligated with a suture, divided, and allowed to retract down into the mediastinum. With this method, the segment of nerve removed averages 9 cm in length (see Figure, F). The area around the cricopharyngeus is sutured back to the esophageal musculature with chromic sutures. This allows for a mild inflammatory response in this region, sealing off the inlet into the laryngeal musculature. The patient is usually discharged on the first postoperative day, after removal of the drain.

We have been very reluctant over the last 4 years to use nerve avulsion in patients with spastic dysphonia, owing to the report by Aronson and DeSanto[8] as well as the optimistic picture that had been painted for botulinum toxin injections in the treatment of these patients. Thus, we performed this procedure in only 15 patients over the last 4 years. The average follow-up for this group is now 1.5 years. Although none of these patients has developed recurring symptoms at this point, it is still too early in their follow-up to draw concrete conclusions.

Some have implied that this is a moot topic in that botulinum toxin will most effectively treat all patients with spastic dysphonia, thus antiquating the recurrent laryngeal nerve section in the treatment of this disease. Through our experience with approximately 80 patients undergoing botulinum toxin injection we have noted a subset of patients not well served by this treatment. In approximately 25% of these 80 patients, the duration of effect is too short, resulting in frequent reinjections. A good-quality voice is only present for 50% of this short interval. We feel that neural avulsion will play a major role in the treatment of this group of patients who have failed botulinum toxin treatment.

CONCLUSION

Therefore, on the basis of these early data, we feel that 1) neural regrowth is one mechanism of failure after recurrent laryngeal nerve section for spastic dysphonia; 2) neural avulsion adds no further morbidity over recurrent laryngeal nerve section, while decreasing the likelihood of neural regrowth; and 3) patients with recurring spastic dysphonia after nerve section should be reinvestigated, with a lidocaine block placed just inferior to the cricoid cartilage. If the spasms again disappear, reexploration with neural avulsion of the distal segment is in order.

Although these conclusions are strongly supported by these data, an ongoing follow-up of these patients must and will be reported after an average 3-year follow-up to either support or refute these conclusions.

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ELECTRICAL PACING FOR DYNAMIC TREATMENT OF UNILATERAL VOCAL CORD PARALYSIS

EXPERIMENT IN LONG-DENERVATED MUSCLE

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In order to explore the possibility of clinical application of laryngeal pacing as a treatment for unilateral vocal cord paralysis, we examined the reactivity of atrophic muscle to electrical stimulation in dogs whose recurrent laryngeal nerves were damaged by crushing, dissection followed by resuturing, or a 3-cm neurectomy. The threshold level to induce enough vocal cord adduction reached the maximum at 2 weeks after nerve injury, decreased with time, and never surpassed 7 V in each case. On the basis of results of these preliminary probings, laryngeal pacing was conducted on a dog 15 months after resection of the laryngeal nerve. Adduction of the paralyzed vocal cord for synchrony with the intact cord was achieved by 7 V of electrical stimulation of the thyroarytenoid muscle that was triggered by signals from the cricothyroid muscle.

KEY WORDS — electrical laryngeal pacing, muscle atrophy, recurrent laryngeal nerve paralysis.

INTRODUCTION

Unilateral vocal cord paralysis leads to various degrees of hoarseness or swallowing difficulty. To eliminate these symptoms, the glottal gap caused by the adductive dysfunction of the paralyzed cord should be corrected. Currently, cordal injection or various thyroplasties have been applied generally with good results. As compared with these static treatments, remobilization of the paralyzed cord is more physiologic in nature. Although many attempts to restore dynamic function of the paralyzed vocal cord using a nerve-to-nerve anastomosis[1,2] or neuromuscular transplantation technique[3,4] have been reported, they have failed in wide clinical applications.

As a new approach to remobilizing the paralyzed cord, the authors reported an electrical laryngeal pacing system that was triggered by a signal from the cricothyroid muscle.[5] Acute phase experiments revealed fair adduction of the paralyzed vocal cord, which synchronized with the movement of the intact cord during phonation. However, several problems must be solved for the final aim, clinical application of laryngeal pacing, to be fulfilled. The most serious problem seems to be muscle atrophy after denervation. This research was designed to examine the reactivity of atrophic muscle to electrical stimulation. In addition, the availability of muscle contraction in response to laryngeal pacing after prolonged denervation was also studied in canine vocal cords denervated 15 months prior to the study.

METHOD AND RESULTS

Experiment 1. Three adult dogs were used in the study. Under Nembutal sodium intravenous anesthesia, unilateral recurrent laryngeal nerves were exposed through a midline neck incision and damaged by crushing, dissection followed by resuturing, or a 3-cm neurectomy. The thyroarytenoid muscles of the damaged side of these dogs were subjected to electrical stimulation immediately and 1, 2, 4, 8, and 12 weeks after the injury. The optimal threshold level that gave adequate adduction of paralyzed cords was measured at each point of time.

As shown in Fig 1, each dog exhibited enough vocal cord adduction immediately after the injury even with 3 V of stimulation. However, the threshold level was raised to 7 to 10 V 2 weeks after the injury and declined slowly thereafter. The threshold decline was the slightest in the dog with nerve resection: to a threshold of 7 V.

Experiment 2. Long-term observation was further performed in three dogs with 3-cm resection of the recurrent laryngeal nerves. The thyroarytenoid

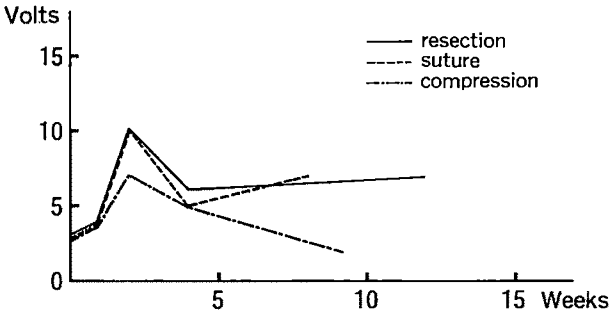

Fig 1. Stimulation voltage for optimal adduction in various types of recurrent laryngeal nerve injuries.

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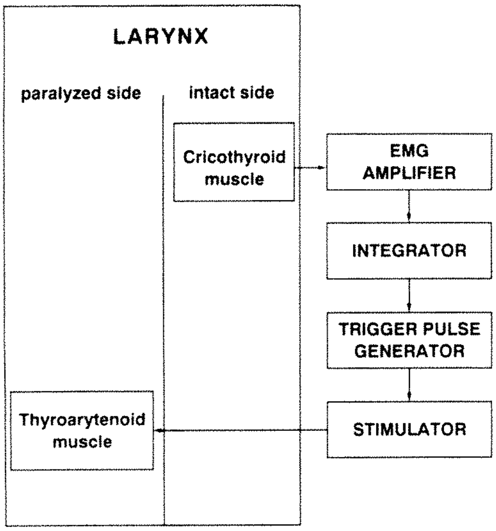

Fig 2. Block diagram of pacing system.

muscle of each dog was subjected to electrical stimulation 10, 14, or 15 months after the injury. The optimal threshold level that gave enough adduction of the paralyzed vocal cord was examined. In each case it exhibited enough adduction with 7 V of stimulation.

Experiment 3. The possibility of laryngeal pacing was examined in the dog used in experiment 2 whose thyroarytenoid muscle had been denervated for 15 months. Under Nembutal anesthesia, the larynx was exposed and a stimulation electrode was inserted into the thyroarytenoid muscle of the paralyzed side through the thyroid cartilage. To attain the trigger signal that synchronized with phonation, a wire electrode was set in the cricothyroid muscle of the intact side. After integration of the electrical discharge from the cricothyroid muscle, the difference in the level of the signal during phonation and during respiration was used for setting the threshold. The waveform of the electrical stimulation used was monophasic and rectangular, with a frequency of 50 Hz, a duration of 5 milliseconds, and a voltage of 7 V (Fig 2). In addition, the larynx after the laryngeal pacing experiment was submitted to histologic examination (Fig 3).

In contrast to the intact side, muscle atrophy of the paralyzed side was obvious. This experiment, which was designed to examine the availability of laryngeal pacing in such severely atrophic muscle, revealed that remobilization of the paralyzed cord in synchrony with the intact cord was possible even 15 months after denervation.

One cycle of adduction-abduction during electrical pacing is shown in Fig 4. The paralyzed side is on the left. Slight asynchrony was noted between the two cords. Although the intact cord has apparently started adducting already, the paralyzed one appears not yet to be initiating any movement in Fig 4, part 2. In Fig 4, part 3, adduction of the paralyzed cord is observed and complete closure is obtained. On glottal opening, the paralyzed side also lagged behind the intact one.

DISCUSSION

Although a number of research and clinical attempts that aim at remobilizing the paralyzed vocal cord have been proposed, the methods of nerve-to-nerve anastomosis and neuromuscular transplantation are still far from clinical application. On the other hand, electrical stimulation has recently been used to treat muscle palsy,[6] and it is being experimentally applied in the larynx.[7,8]

We previously reported[5] on the electrical pacing of vocal cord adduction triggered by electrical discharge from the cricothyroid muscle, with some

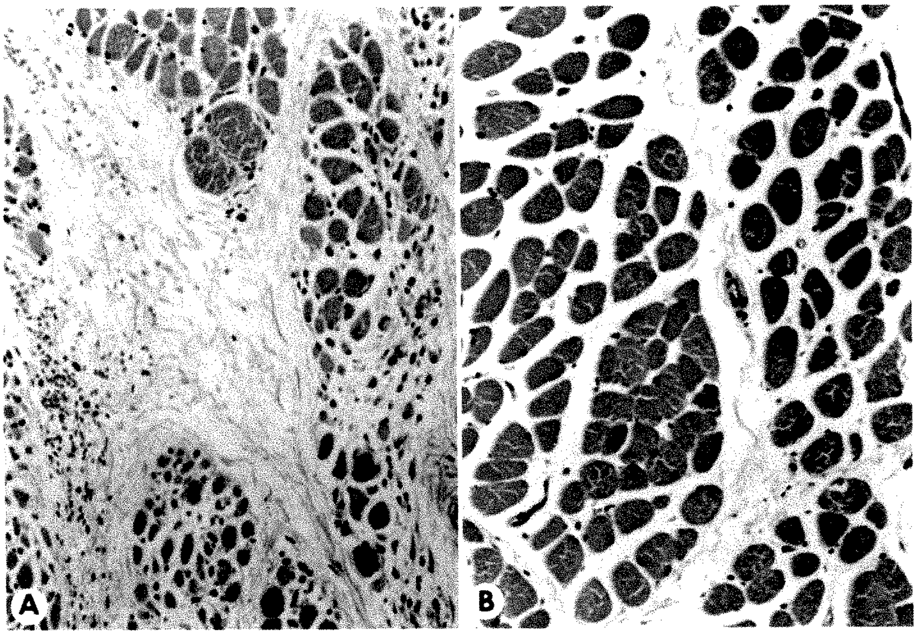

Fig 3. Histologic findings of thyroarytenoid muscle. A) At 15 months after denervation, distinct muscle atrophy is observed. B) Intact side.

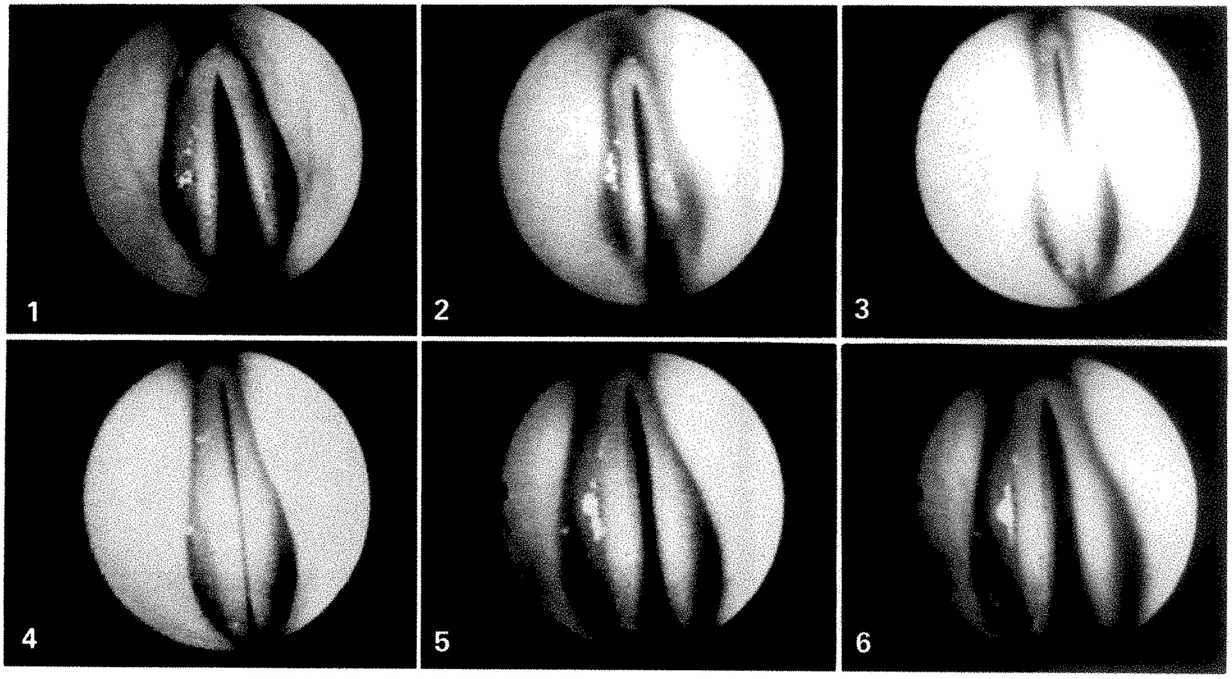

Fig 4. One cycle of adduction and abduction during electrical pacing.

promising results in the acute experiment. This procedure, however, involves several unsolved problems concerning, for example, miniaturization of the tools, biocompatible material for long-term implantation, and muscle atrophy after denervation. Among these problems, here discussed are atrophic muscle after denervation and its reactivity to electrical stimulation. According to Sato's[9] report, the level of stimulation voltage for the maximum contraction of the thyroarytenoid muscle reached the maximum in 2 or 3 weeks after the denervation, and it would be 30 V. Such a high stimulation voltage could be painful, making it impossible to apply the laryngeal pacing. Even if it were possible, such stimulation would cause a leak of electrical current into the trigger electrode placed in the intact cricothyroid muscle, thereby disrupting the synchrony between the two vocal cords. We investigated the threshold voltage of stimulation to induce enough glottic closure under various conditions of nerve palsy. The results were almost in agreement with Sato's, with the threshold level reaching the maximum at 2 weeks after nerve injury. However, the level decreased with time, and it never surpassed 7 V even in the worst case of nerve resection.

In order to reveal the stimulation voltage required for long-denervated atrophic muscle, laryngeal pacing was conducted on a dog 15 months after resection of the recurrent laryngeal nerve. Adduction of the paralyzed cord for phonation in synchrony with the intact cord was induced by 7 V stimulation. Concerning the time lag between the two cords, we observed that the stimulated vocal cord lagged slightly behind the intact one, as we had reported previously in the acute-phase experiment. This time lag may be attributable to the integrating time of the action potential of the cricothyroid muscle in the closing phase, and to the passive glottic movement in the opening phase. Muscle atrophy in the chronic-phase experiment seemed to have no effect on this time lag. Taking into consideration the ability of continuous electrical stimulation to prevent muscle atrophy as reported by Lomo and Rosenthal,[10] Westgaard,[11] and Pachter et al,[12] we can conclude that the result of this chronic experiment would indicate laryngeal pacing as being one of the potential treatments for unilateral vocal cord paralysis.

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INTERNATIONAL HEARING AID CONFERENCE: SIGNAL PROCESSING, FITTING, & EFFICACY

The International Hearing Aid Conference: Signal Processing, Fitting, & Efficacy will be held June 21-23, 1991, at The University of Iowa, Iowa City, Iowa. The organizing committee includes Richard S. Tyler, PhD (Signal Processing), Chaslav V. Pavlovic, PhD (Fitting), and Ruth A. Bentler, PhD (Efficacy). Further information may be obtained from any member of the organizing committee at the Department of Speech Pathology and Audiology, The University of Iowa, Iowa City, IA 52242; (319) 335-8726, FAX (319) 335-8851.

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SUPRAGLOTTIC CONTRIBUTIONS TO PITCH RAISING

VIDEOENDOSCOPIC STUDY WITH SPECTROANALYSIS

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Several questions pertaining to pitch raising recur frequently. Does the larynx rise with the production of higher frequencies? What happens to the pharyngeal walls between the soft palate and the larynx when the fundamental frequency is raised? How does the soft palate participate in pitch raising? To answer these questions, the present study was undertaken with the recently described simultaneous velolaryngeal endoscopy technique. Nine professional singers were asked to find the limits of their vocal range in any of six voice qualities: speech, falsetto, cry/sob, twang, belting, and opera. Simultaneous activities of the larynx, the pharyngeal walls, and the soft palate were submitted to videoendoscopy with synchronous voice recording and studied with spectroanalysis of discrete segments of the total phonation range. Our dual endoscopic study showed that 1) the larynx rose in all subjects with the production of higher frequencies, 2) with the highest fundamental frequency, the lateral pharyngeal walls significantly contracted toward the midline in an "upside-down V shape," creating a very narrow pharyngeal tube, and 3) the soft palate lifted and the velopharyngeal port narrowed considerably with higher frequencies.

KEY WORDS — laryngeal height, pharyngeal walls, pitch raising, simultaneous velolaryngeal endoscopy, velar elevation.

INTRODUCTION

Several questions pertaining to pitch raising recur frequently. Does the larynx rise with the production of higher frequencies? What happens to the pharyngeal walls between the soft palate and the larynx when the fundamental frequency (F0) is raised? How does the soft palate participate in pitch raising?

Many investigators have studied the velopharyngeal mechanism using a number of research modalities, including tomography,[1-5] cinefluorography and videofluorography,[6-13] electromyography,[14-18] and ultrasonic measurement.[19-22] With the development of endoscopy, however, the instrumentation itself has literally thrown light into the poorly understood aspects of vocal physiology.[23-32]

While studying the role of the soft palate in laryngeal functions with the simultaneous dual velopharyngeal endoscopy technique,[31] the authors realized that this technique might prove useful for the investigation of the supraglottic participation in pitch raising. The purpose of this paper is to examine laryngeal height, pharyngeal wall movement, and the activity of the soft palate in pitch raising by use of the recently described simultaneous velolaryngeal endoscopy technique and acoustic analysis.

MATERIAL AND METHOD

SUBJECTS

Nine professional singers and two untrained subjects participated in the dual velolaryngeal endoscopic procedure to record the limits of their frequency range. Of the singers, four were men and five were women. The untrained subjects were both men. The ages ranged from 25 to 69 years (mean, 40 years). Only one woman could not tolerate the telescopic procedure because of unusually narrow nasal passages.

EQUIPMENT

The following equipment was used for this study: 1) an Olympus ENF-P2 flexible fiberscope; 2) a Hopkins 70° rigid telescope (Karl Storz 7200C); 3) xenon cold light fountains (Karl Storz 487C); and 4) video cameras [1) an Elmo EM-102 micro CCD color video camera (15 lux) attached to the flexible fiberscope; 2) a Ricoh CCD R-620 home color video camera (4 lux) attached to the Hopkins 70° rigid telescope; and 3) an Ikegami ITC 730AP camera, to videotape the overview picture of the procedure] and two monitors placed side by side showing the simultaneous images of the soft palate and the larynx; 5) Sony ¾-in VO-5600, VO-5800, and VO-5850 video recorders; 6) an Electro-voice RE-10 unidirectional microphone; 7) a Sony UP-811 videographic printer; and 8) for the acoustic analysis, a Sun 4-110 computer with proprietary software developed at AT&T Bell Laboratories.

TECHNIQUE

The technique of simultaneous velolaryngeal endoscopy used for this study was the same as that described by Yanagisawa et al[31] (Fig 1).

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Presented at the meeting of the American Laryngological Association, Palm Beach, Florida, April 28-29, 1990.

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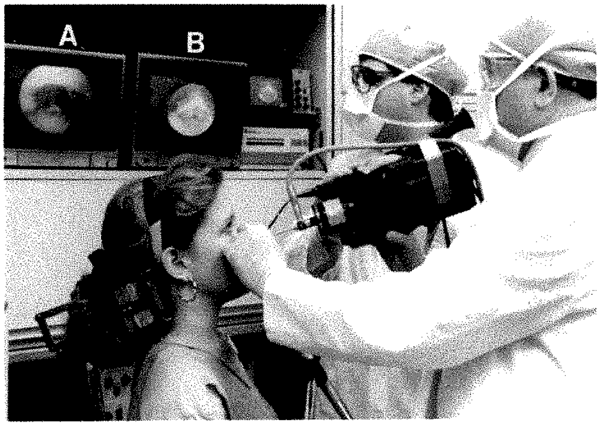

Fig 1. Technique of simultaneous fiberscopic and telescopic velolaryngeal endoscopy. A — monitor 1 (telescopic image), B — monitor 2 (fiberscopic image).

The subject sat facing the examiner and the assistant. Topical anesthesia and vasoconstriction were achieved with aerosolized 4% lidocaine hydrochloride (Xylocaine) and 3% ephedrine sulfate. In addition, a pledget soaked with 4% lidocaine solution and 3% ephedrine was placed for 5 minutes in the right side of the nasal cavity for easy passage of the rigid telescope.

Simultaneous velolaryngeal videoendoscopy was performed as follows. The Olympus ENF-P2 flexible fiberscope was first passed through the left nasal cavity down to the pharynx. When the ideal image of the larynx was obtained on monitor 2 (fiberscopic image) (Fig 1), the fiberscope was fixed to the nose with adhesive tape to minimize the vertical motion of the distal end of the scope. The fiberscope, to which the first video camera was attached, was then handed over to the assistant, who held the fiberscope and the camera during the entire procedure. The Hopkins 70° rigid telescope, to which the second video camera was attached, was then passed into the right nostril. While viewing monitor 1 (telescopic image) (Fig 1), the operator carefully and slowly passed the scope into the nasopharynx, and the optimal image of the upper surface of the soft palate and the velopharyngeal sphincter was obtained.

During the videotaping procedure, three separate images were recorded on three separate $^3/_4$-in video cassettes: 1) the fiberscopic view (monitor 2), 2) the telescopic view (monitor 1), and 3) an overview of the procedure taken by the third camera, which included the simultaneous view of monitors 1 and 2. All the recordings were made on the Sony $^3/_4$-in VO 5600 and VO 5800 recorders.

Audio and Video Synchronization. During the procedure, the subject's voice was recorded simultaneously on each videotape recorder (Sony VO 5600 and VO 5800) on audio track channel "2" with use of a single unidirectional microphone placed 7.5 cm (3 in) diagonal to the subject's mouth. To aid in synchronization of the two diagnostic images, a time code from a single time code source was recorded simultaneously on audio track channel "1" of each videotape recorder, thus making it possible to match the telescopic and fiberscopic images quickly and accurately to the exact frame during editing.

In order to view the telescopic and fiberscopic images simultaneously on a single screen, it was necessary to reposition and reduce the size of both images. With a Microtime RP-1 three-dimensional digital effects generator, first the telescopic image was positioned on the left of the screen, and then the fiberscopic image on the right. The left and right images and both audio channels (channel "2" containing the subject's voice, and channel "1" containing the time code information) were rerecorded onto the new submaster on a Sony BVW-75 Betacam SP video cassette recorder to maintain the highest possible picture quality. A Sony BVE-900 automatic electronic editing controller and the Grass Valley 100 special effect generator were used to produce the final dual image tape in perfect synchronization for analytic review.

PROTOCOL

The protocol was in two parts. In part 1, the purpose was to examine the larynx, pharyngeal walls, and soft palate at all parts of the total frequency range. For this purpose each subject was asked to siren as high and as low as possible on an "ng" sound. (A siren is a continuous glide [glissando] from one pitch to another.) With the nasal "ng," the soft palate is lowered, allowing visualization of the vocal tract from the position of the velopharyngeal port. Another advantage to using an "ng" instead of any other nasal or vowel sound is that with the "ng," the tongue is in its highest position, minimizing any tongue interference with the movement of the larynx upward in the execution of the highest frequency range. In part 2, for purposes of comparing across subjects and for acoustic analysis, discrete frequencies were recorded at 10%, 25%, 50%, 75%, and 90% of the subject's total range.

To observe differences in function imposed by the constraints of different voice qualities, the subjects were asked to choose from the following six different genres of music: speech, falsetto, cry/sob (a very dark, repressed, "covered" sound), twang (heard in American country-western music), belting (heard in Broadway theater and in ethnic music around the world), and opera.[18,31,33-36]

Not all subjects recorded all qualities, nor was it possible in all trials to capture the simultaneous activity of all the structures. Nevertheless, all subjects with several practice trials were successful in sirening the total range. From the one subject whose nasal passages would not permit the dual endoscopic procedure, data were obtained with the fiberscope positioned above and then below the soft palate.

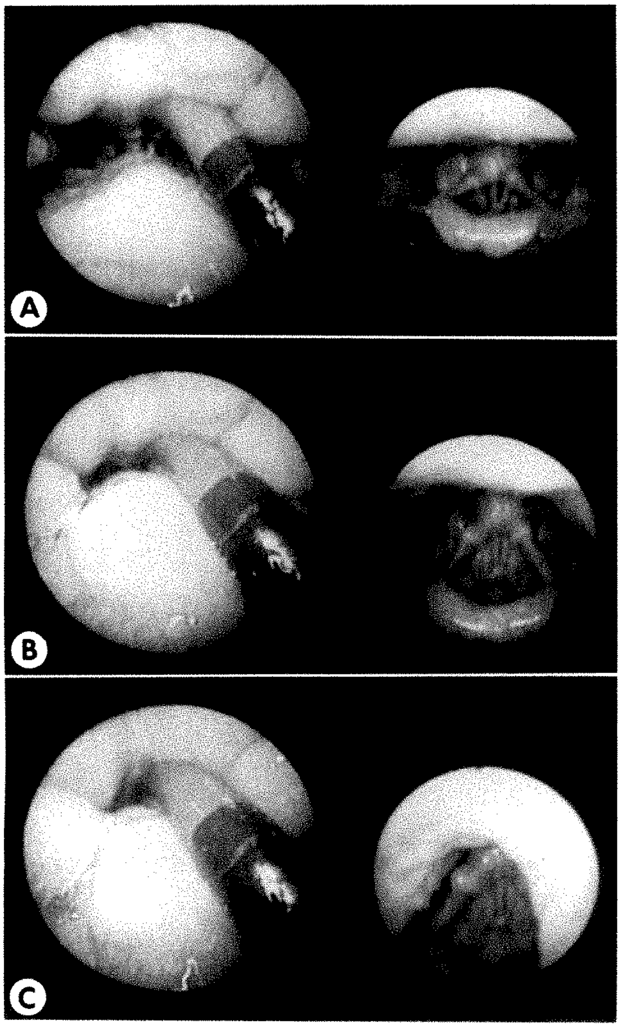

Fig 2. Criteria for judging laryngeal height. A) Lowest and smallest larynx (right, fiberscopic image) and open velopharyngeal port (left, telescopic image). B) Middle height of larynx (right, fiberscopic image) and partially open velopharyngeal port (left, telescopic image). C) Highest and largest larynx (right, fiberscopic image) and almost closed velopharyngeal port (left, telescopic image).

METHOD OF ACOUSTIC ANALYSIS

The audio signals were digitized at 12 kHz with a 16-bit linear converter after being low-pass filtered at 5.8 kHz. They were then digitally filtered at 5 kHz with a brick-wall finite impulse response filter and down-sampled to 10 kHz. Computer-generated broadband spectrograms were made of the target vocalizations. The spectrograms and time waveforms were studied to select steady-state segments that reflect the spectral characteristics of each token. The vibrato frequency for the subject in question was approximately 5 Hz. The Hanning analysis window of 200 milliseconds' duration was chosen to be approximately equal to the vibrato period. When a token exhibited vibrato, the window was centered on the minimum-frequency part of the vibrato cycle. No preemphasis was used prior to spectral analysis, so that the results reflect the actual vocal source and radiation characteristics. The ordinate of the spectral plots is in decibels re an arbitrary but constant reference.

CRITERIA FOR VIDEOENDOSCOPIC ANALYSIS

Criteria for Characterizing Laryngeal Height (Fig 2). The values attributed to laryngeal height were subject-dependent. The position of the fiberscope relative to the nose was constant, since the scope was taped to the nose. When the larynx moved down, the distance between the larynx and the tip of the fiberscope increased and the image of the larynx became smaller on the screen (Fig 2A). Just the opposite occurred when the larynx was raised (Fig 2C). The lowest position of the larynx that corresponded to the smallest image was assigned a 1 (Fig 2A), and the highest position, and hence the largest image, was chosen as 5 (Fig 2C) for each subject over the entire range of voice qualities each was able to perform. Thus, no matter what the excursion of movement a subject might display, his lowest position was always a 1, and his highest, a 5.

Criteria for Characterizing Pharyngeal Wall Constriction. These were as follows.

1 — wide open pyriform sinus (Fig 3A).
2 — partial closure of pharyngeal walls with floor of pyriforms still visible (Fig 3B).
3 — pyriforms nearly closed, obstructing view of floor (Fig 3C).
4 — obliteration of pyriform sinus (Fig 3D).
5 — complete covering of aryepiglottic folds by pharyngeal walls (Fig 3E).

Criteria for Characterizing Soft Palate Elevation. These were as follows.

1 — wide open velopharyngeal port with larynx visible (Fig 4A).
2 — open velopharyngeal port with larynx partially visible (Fig 4B).
3 — only uvula touching posterior pharyngeal wall (Fig 4C).
4 — wide soft palate–posterior pharyngeal wall contact with minimal lateral openings (Fig 4D).
5 — complete velopharyngeal closure (Fig 4E).

The values recorded for any condition had to be agreed on unanimously by the three senior authors. When a difference of opinion occurred, prints were made with a Sony UP 811 and direct comparisons were made with the models set a priori for numerical judgments. To aid in making judgments, the slow motion study of video images was also done with the Sony VO 5850 editing recorder/player, which has an ultraslow motion and freezing capability.

RESULTS

From the master tape of the video recordings of the tokens of sirens (glissandos) and of discrete F0s, the authors made judgments on the exposure of the

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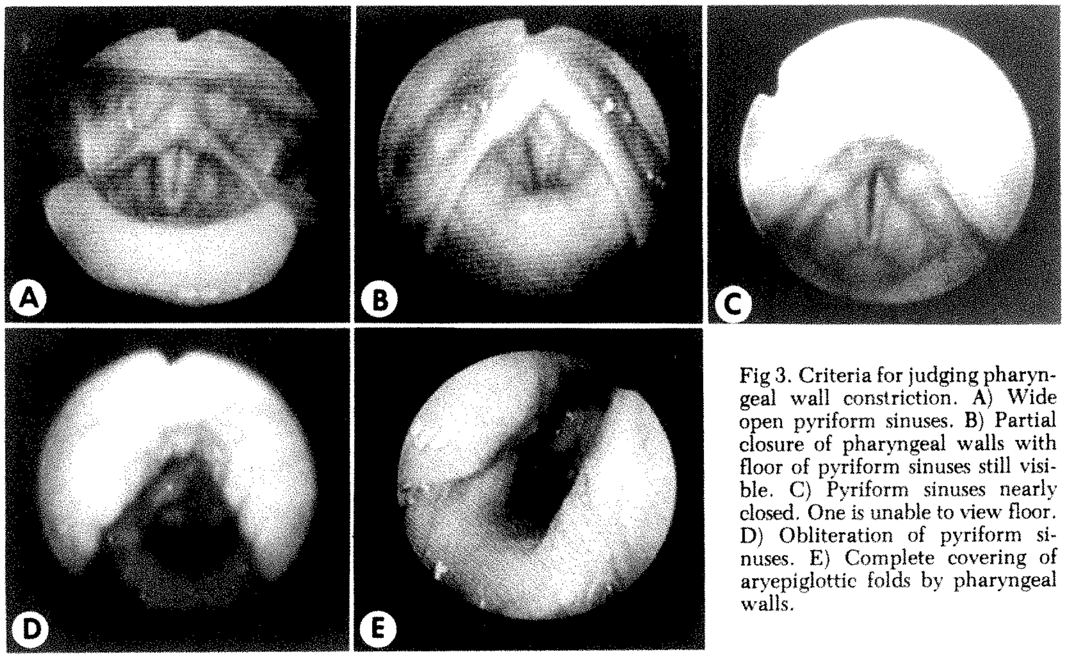

Fig 3. Criteria for judging pharyngeal wall constriction. A) Wide open pyriform sinuses. B) Partial closure of pharyngeal walls with floor of pyriform sinuses still visible. C) Pyriform sinuses nearly closed. One is unable to view floor. D) Obliteration of pyriform sinuses. E) Complete covering of aryepiglottic folds by pharyngeal walls.

anatomic structures of the best trials of each subject that also presented the clearest pictures. The results of these judgments are presented in the Table, in which the subjects are listed by voice classification (soprano, baritone, bass, or tenor), by their total phonational range in semitones (STs; an ST is one 12th of an octave; two adjacent keys on a piano are an ST), and by the voice quality most comfortable for each subject. The three columns that follow record the subjective evaluation of the conditions of laryngeal height, pharyngeal wall closure, and soft palate. Within each column are values for three parts of the total phonation range: the extreme bottom (0%), the middle (50%), and the highest Fo (100%).

TOTAL PHONATION RANGE (EIGHT SUBJECTS)

The data in the Table are displayed in Fig 5.

Laryngeal Height. For all subjects, no matter what their voice quality or what the extent of vertical excursion, the larynx rose to its highest position for the highest F0. As F0 increased, all subjects raised the larynx for each higher F0, except subject EL, whose larynx displayed the least movement from the lowest to highest pitch. However, she, too, raised the larynx at the highest level of her range.

Pharyngeal Walls. For all subjects, the pharyngeal walls were most constricted at the highest F0. As F0 increased, the walls, beyond midrange, began to close, and by the highest F0 in some of the sub-

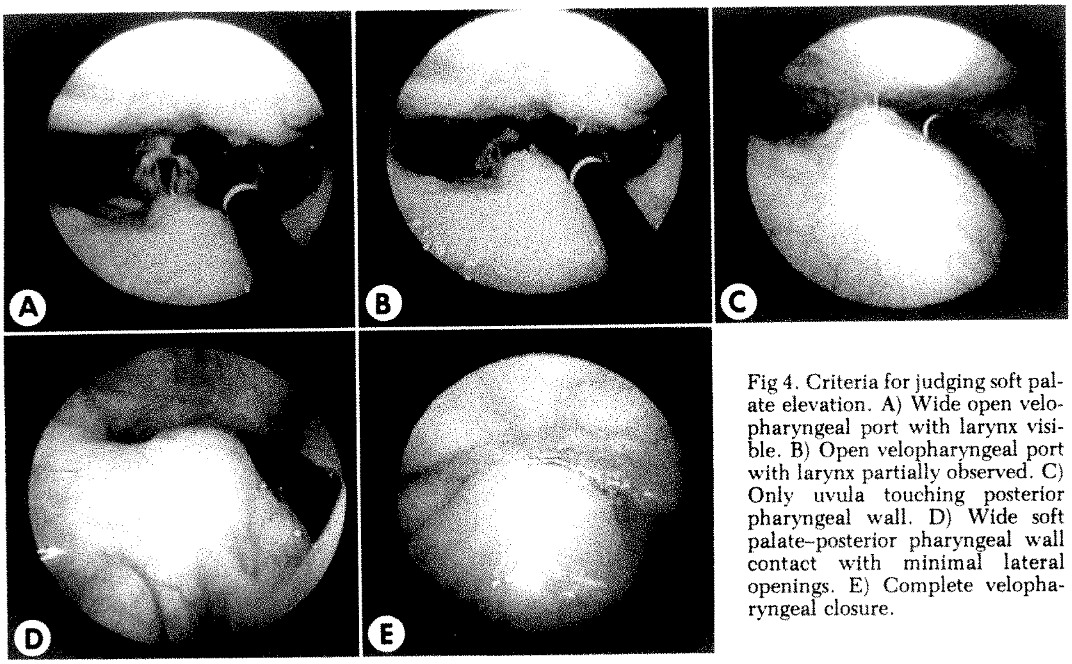

Fig 4. Criteria for judging soft palate elevation. A) Wide open velopharyngeal port with larynx visible. B) Open velopharyngeal port with larynx partially observed. C) Only uvula touching posterior pharyngeal wall. D) Wide soft palate–posterior pharyngeal wall contact with minimal lateral openings. E) Complete velopharyngeal closure.

SUPRAGLOTTIC RELATIONSHIPS BY SUBJECT

Subject	*Voice*	*Phonation Range (ST)*	*Quality*	*Laryngeal Height Range (%)* 0	50	100	*Pharyngeal Walls Range (%)* 0	50	100	*Soft Palate Range (%)* 0	50	100
Professional singers												
AB	Bari	37	Speech	1	3	5	1	1	3	3	2	4
			Falsetto	2	3	4	1	1	3	3	3	4
			Sob	1	2	4	2	1	4	3	2	4
			Twang	1	2	3	3	2	4	1	3	4
			Opera	1	2	4	2	1	4	3	2	4
TC	Bari	37	Speech	1	3	5	3	1	2	2	1	4
			Falsetto	1	3	5	3	2	2	2	3	3
			Sob	1	2	4	2	1	4	1	3	4
			Twang	?	3	?	4	3	5	2	3	4
			Opera	2	3	4	3	1	4	2	2	3
JE	Sop	34	Speech	2	3	5	2	3	4	2	3	4
			Falsetto	2	3	5	2	2	4	2	3	4
			Sob	1	3	5	2	2	4	3	4	4
			Twang	2	3	5	3	4	5	3	3	4
			Opera	1	3	5	2	3	4	3	4	4
JB	Sop	37	Opera	1	3	5	1	3	5	1	3	4
EL	Sop	37	Opera	1	1	5	2	3	4	3	3	4
BG*	Sop	27	Opera	1	2	5	2	2	3	1	2	4
MH	Sop	39	Speech	1	3	5	2	3	4	1	3	4
JS	Bari	34	Opera	1	3	5	1	3	4	1	2	3
SG	Bari	35	Opera	1	3	5	2	1	4	1	2	3
Nonprofessional singers												
DT	Bari	34	Speech	1	3	5	1	3	5	1	2	4
SK	Tenor	29	Speech	1	3	5	2	1	3	2	1	3

Scale from 1 to 5: laryngeal height — 1 = lowest, 5 = highest; pharyngeal walls — 1 = most open, 5 = most closed; soft palate — 1 = most open, 5 = most closed.

Bari — baritone, Sop — soprano, ST — semitone.

*Subject could not tolerate dual procedure. Palate data from fiberscopic examination above and below palate.

jects the walls appeared to be no wider than the width of the aryepiglottic rim (Fig 3D,E). In two subjects, JB and DT, the pharyngeal walls appeared to "wrap around" and almost cover the aryepiglottic rim (Fig 3E). In two subjects, SG and SK, the pharyngeal wall closure was delayed well beyond midrange, but these subjects also constricted for the highest F0. At the lowest part of the range, pharyngeal wall closure was mixed. In four subjects (all men), the pharyngeal walls constricted from the position at 50% of the range to form the lowest F0. Five subjects (four women, one man) widened their pharyngeal walls at the lowest part of the range. One woman stayed the same while another woman either opened her pharyngeal walls or kept them the same depending upon the voice quality performed.

Soft Palate. For all subjects, the soft palate was most elevated and the velopharyngeal port was

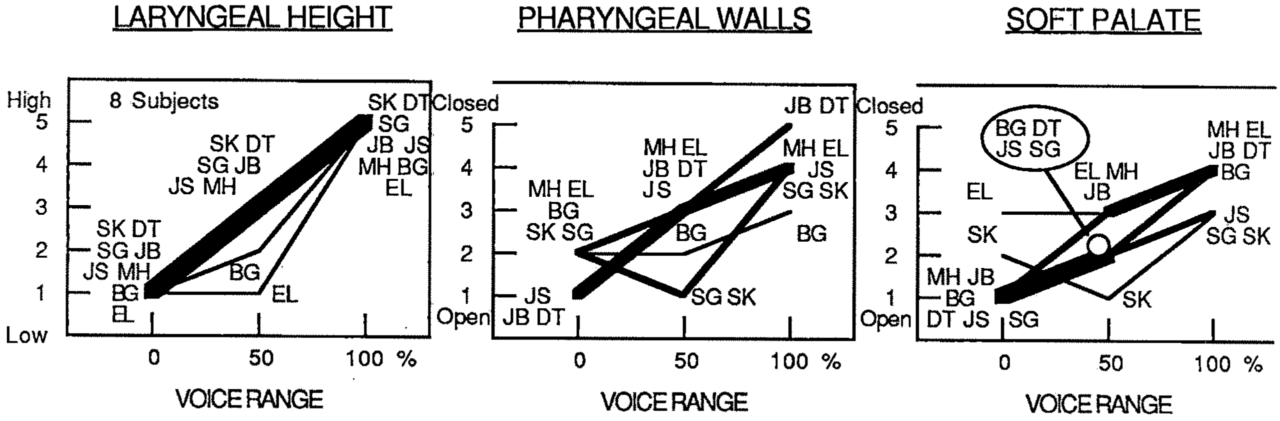

Fig 5. Comparison of supraglottic dynamic behavior of laryngeal height, pharyngeal wall constriction, and soft palate elevation of eight subjects. Subjects JB, EL, BG, JS, and SG all sang in opera quality while MH, DT, and SK sang in speech quality. Data, from Table, represent conditions at midpoint and end points of voice range of each subject.

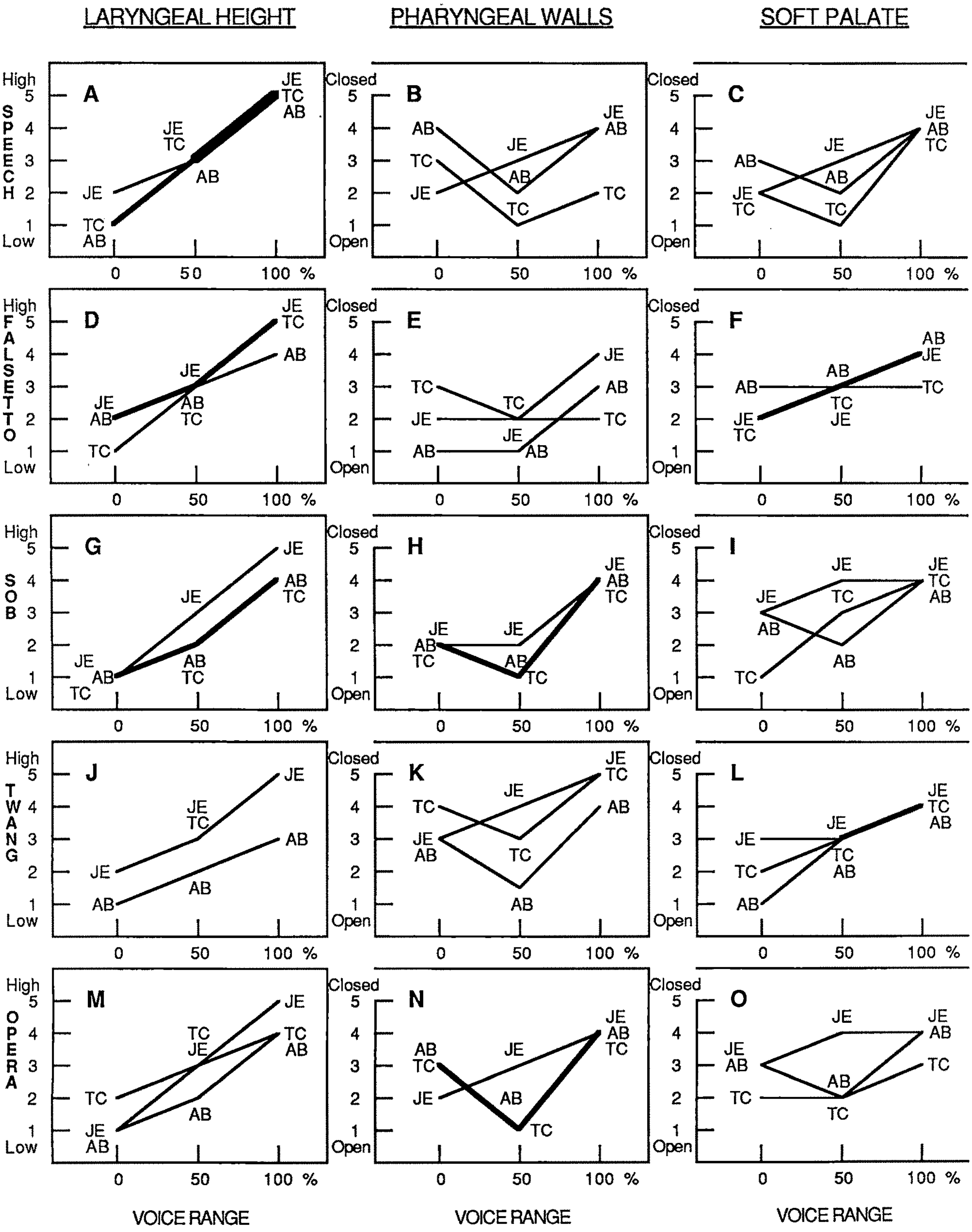

Fig 6. Comparison of supraglottic dynamic behavior of laryngeal height, pharyngeal wall constriction, and soft palate elevation in five qualities — A-C) speech, D-F) falsetto, G-I) sob, J-L) twang, and M-O) opera — as three subjects (AB, TC, and JE) sang "ng" at middle and extreme ends of range.

most closed at the highest end of the range. For most subjects, at the lowest part of the frequency range, the soft palate was lowest and the velopharyngeal port most open.

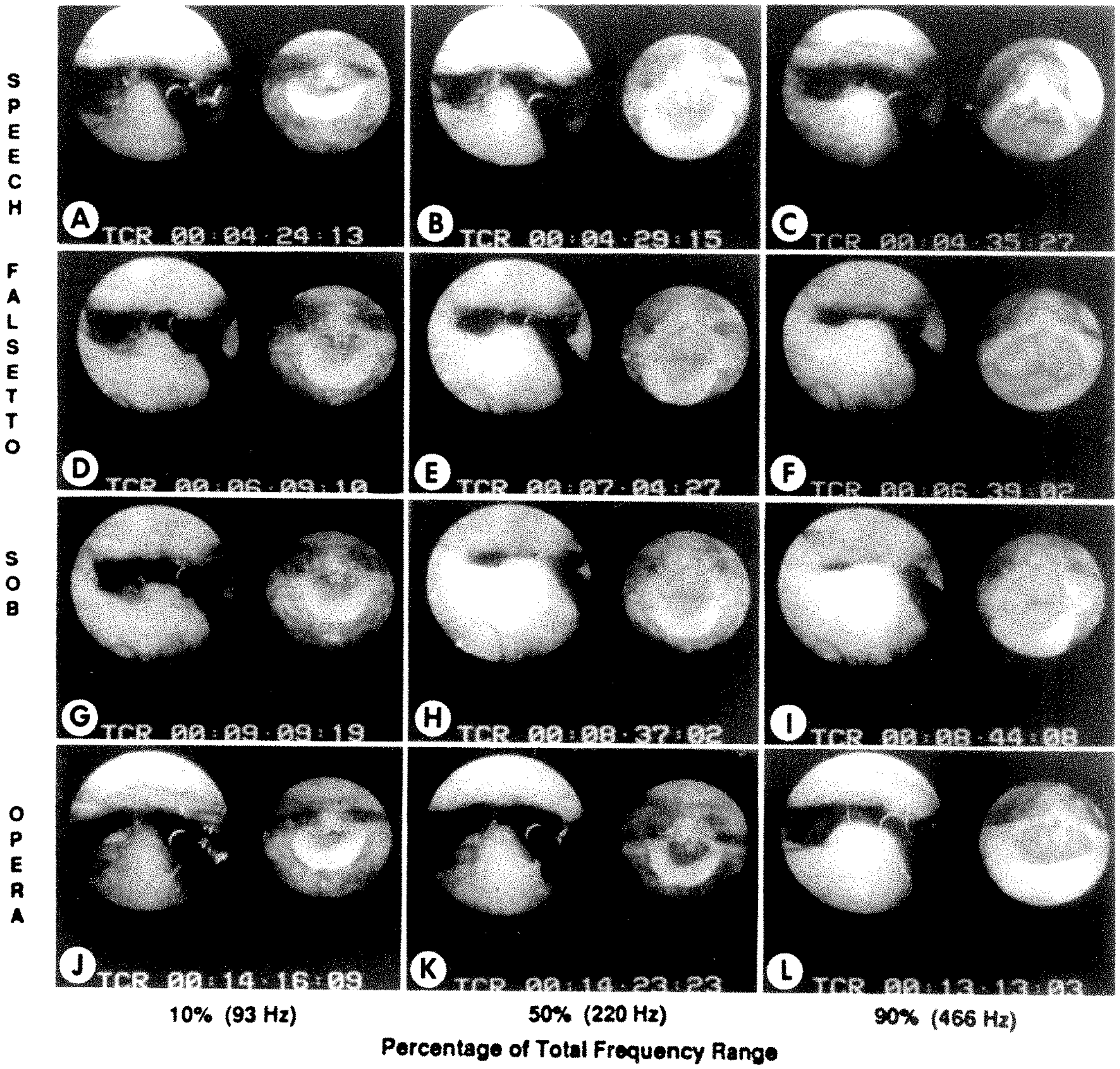

Fig 7. Photographs of velopharyngeal sphincter and larynx in four voice qualities of subject TC as he sang "ng" at three parts of his total voice range at 10% (93 Hz), 50% (220 Hz), and 90% (466 Hz). A-C) Speech. D-F) Falsetto. G-I) Sob. J-L) Opera.

COMPARISON OF VOICE QUALITIES (THREE SUBJECTS)

Three subjects (TC, AB, and JE) were able to record five qualities: speech, falsetto, sob, twang, and opera. The data are included in the Table and are displayed in Fig 6. Qualities are displayed horizontally in rows with speech (Fig 6A-C) at the top, followed by falsetto (Fig 6D-F), sob (Fig 6G-I), twang (Fig 6J-L), and opera (Fig 6M-O). Data for the three anatomic structures are displayed vertically in columns with laryngeal height at the left (Fig 6A, D,G,J,M), pharyngeal walls in the center (Fig 6B, E,H,K,N), and soft palate at the right (Fig 6C,F, I,L,O). Within each cell the subjective analysis is on the ordinate and values for the F0 at 10%, 50%, and 100% of frequency range are on the abscissa.

In general there were similar results for all three structures at the highest end of the range. The larynx was highest, the pharyngeal walls were most closed, and the soft palate was most elevated at 100% of the total range.

No quality displayed a pattern exactly like that of any other quality. As one compares the data vertically for each of the three structures, there is also no pattern evident across the range for any single quality for any single subject. In only one cell (Fig 6D) was there total agreement among three subjects. Figure 6J had incomplete data for subject TC, whose structures were obscured in twang quality at the lowest and highest F0s. For subject JE (a woman), 10 of the 15 cells showed a positive linear slope.

COMPARISON OF FOUR QUALITIES (ONE SUBJECT)

To examine more closely differences in quality, we compared four qualities — speech, falsetto, sob, and opera — in one subject (TC). In Fig 7, again, quality is displayed horizontally in rows with speech in Fig 7A-C, falsetto in Fig 7D-F, sob in Fig 7G-I, and opera in Fig 7J-L. Displayed in the verti-

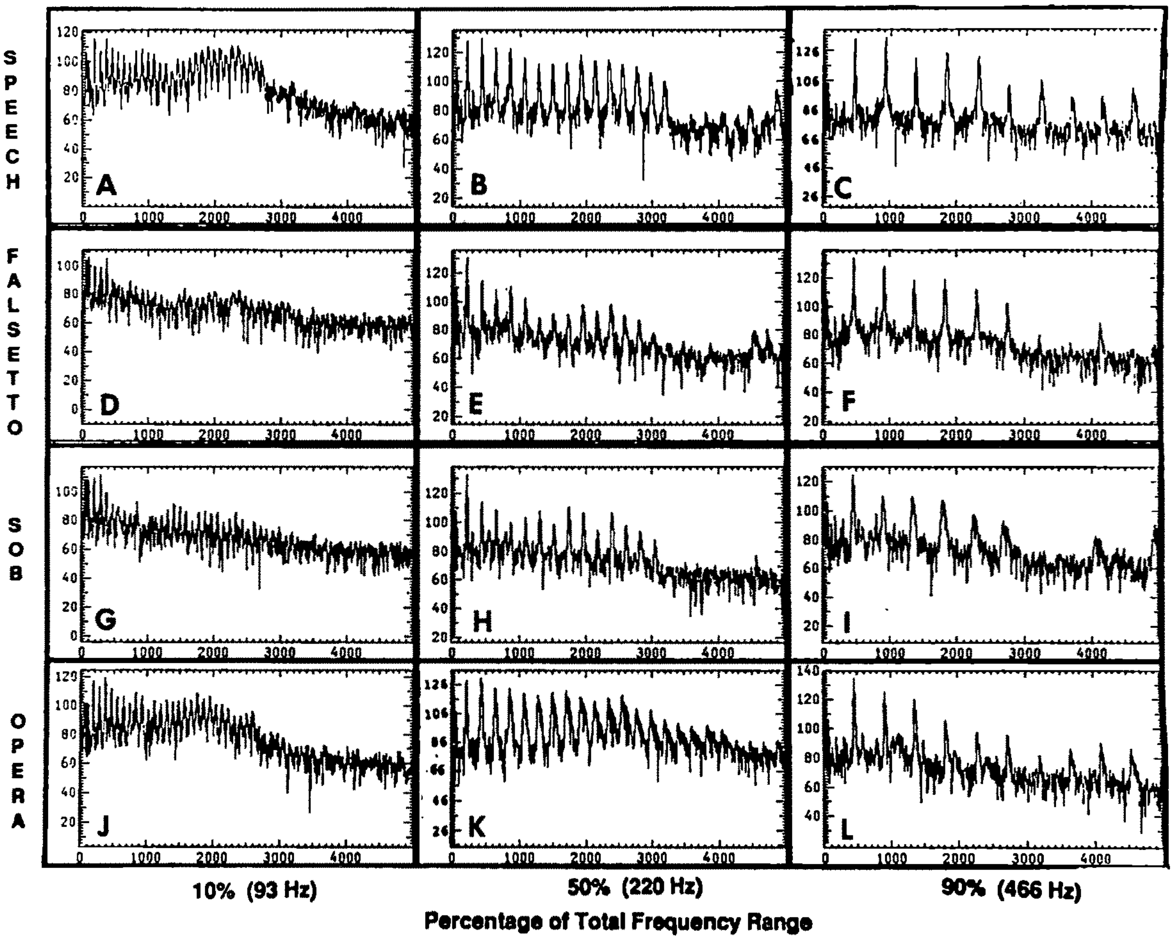

Fig 8. Acoustic analysis of subject TC comparing "ng" in four qualities at three parts of total voice range at 10% (93 Hz), 50% (220 Hz), and 90% (466 Hz). Each cell displays amplitude on ordinate and spectrum (1 to 5 kHz) on abscissa. A-C) Speech. D-F) Falsetto. G-I) Sob. J-L) Opera.

cal columns are parallel views of the soft palate on the left and the larynx on the right for three discrete frequencies at 10% (93 Hz; Fig 7A,D,G,J), 50% (220 Hz; Fig 7B,E,H,K), and 90% (466 Hz; Fig 7C,F,I,L) of this subject's total range of 37 STs.

Laryngeal Height. When the actual pictures are arranged for simultaneous comparison, certain observations can be made that were not possible in the analysis of Fig 6. For example, laryngeal height, as judged by its proximity to the camera (the tip of the fiberscope), was seen to be farthest from the camera at 10% (Fig 7A,D,G,J) and closest at 90% (Fig 7C,F,I,L). Moreover, as F0 increased to 90% of the frequency range, there appeared to be a forward or anterior tilt of the larynx, as judged by the position of the epiglottis and arytenoids (Fig 7C,F,I,L).

Soft Palate and Uvular Muscle Elevation. In all qualities, the soft palate was more elevated at 90% than at 10% of the range (Fig 7C,F,I,L). The uvular muscle rises as F0 increases from 10% to 90%, as judged by its proximity to the camera and by the highlighted or overexposed video images of the superior surface of the soft palate (Fig 7E,F,H,I,L).

Comparing Individual Qualities. It appeared that falsetto and sob qualities were more alike in their characteristics, while speech and opera shared features. In falsetto and sob qualities, more of the vocal folds was exposed at all F0s (Fig 7D-I). Also, soft palate elevation was greater for these two qualities (Fig 7E,F,H,I). In speech and opera, as F0 increased, there was slightly more aryepiglottic tightening, more pharyngeal wall closure, and more tilting of the whole laryngeal structure at 90% than in falsetto and sob qualities (Fig 7C,L).

ACOUSTIC ANALYSIS

In Fig 8, the cells correspond to the photographs in Fig 7, with quality displayed in horizontal rows and F0 in the vertical columns. In each cell is a spectral display of the "ng" sound recorded, with relative amplitude on the ordinate and frequency in kilohertz on the abscissa.

For the subject in question, these points in the range were found to be 90 Hz, 222 Hz, and 461 Hz, respectively, which correspond (±5 Hz) to the F0 targets of 93 Hz, 220 Hz, and 466 Hz the subject attempted. A characteristic common to most of the spectra was the rather abrupt falloff in energy between 2.5 and 3.5 kHz. The hypothesis that this was due to filtering of the "ng" vocalization was largely supported by the observation that the location of the falloff was relatively independent of quality and range. The fact that it did vary within a given voice quality (ie, speech) suggested a change in the vocal tract configuration such as velar port opening, pharyngeal constriction, or larynx height. The location and movement of this falloff with range change appeared similar for the conditions represented by the first three rows of plots. The fourth row (opera) exhibited qualitatively different behavior, possibly owing to the singer's vocal strategies designed to enrich the higher harmonics in opera quality when singing vowels.

The falsetto and sob qualities were distinguished throughout their ranges by having relatively high-energy first harmonics. As might be expected, the speech quality exhibited a smaller spectral slope below 3 kHz than did the sob or falsetto qualities. Surprisingly, however, at 90 Hz and at 222 Hz, the slope for this example of speech quality had a slower rate of rolloff than that of the opera tokens.

DISCUSSION

LARYNGEAL HEIGHT

One of the earliest references to laryngeal height was made by Berard in 1755,[37] who noted by palpation that his laryngeal height could be correlated with increasing degrees (lines and spaces) on the musical staff. Many different opinions were expressed regarding the rise of the larynx with increasing F0. They differed depending on whether the subjects being tested were trained or untrained,[28,38] whether the pedagogic opinion favored one acoustic condition over the other,[28,39-41] or whether aesthetic, cultural, or personal choice determined the quality.[35,39,42] Other investigators have shown that the larynx rises with increasing F0, as determined by x-ray study,[35,43,44] by palpation,[37] by external measurement,[42] and by fiberoptic analysis.[28] In the x-ray studies of Colton and Estill,[35] the x-ray films were taken only one octave apart (294 Hz and 587 Hz or 12 STs). There was a rise in height in three of the four qualities, with some narrowing at the laryngopharyngeal level. The larynx in opera quality did not rise in this lower octave.

In the current study, laryngeal height correlated positively with vocal range: the higher the F0, the higher the larynx. In some subjects (EL, for example) the range of movement was narrower (Fig 5), owing in part to her training as an opera singer, which emphasized a low, stable larynx. Nevertheless, in all subjects, the larynx rose with vocalization at the highest part of the range. It should be mentioned, however, that in choosing the criteria for judging laryngeal height it was difficult to accurately measure the magnitude of vertical excursion from above endoscopically. We determined the laryngeal height by freezing combined telescopic and fiberscopic video images during ultraslow motion review with the Sony VO 5850 recorder/player and by comparison of video printouts of each step of vertical laryngeal motion. At present, videofluoroscopic examination in the lateral projection is probably the most reliable method of making such a measurement.

PHARYNGEAL WALL MOVEMENT

A review of x-ray studies reporting on laryngeal height shows that as the larynx rises, not only is the vocal tract shortened, but the pharyngeal walls contract, making the vocal tract narrower.[44,45] The present study clearly showed the dynamic movement of the vocal tract with changes up or down on the frequency scale. The pharyngeal walls were widest (side to side) in the lower range to middle range and narrowest at the highest range. In both trained and untrained subjects, with the upward movement of the larynx at the higher frequencies, there was also a constriction of the lateral pharyngeal walls in an upside-down V shape (see Table and Fig 5).

Many investigators[4,6,7,8,11,19,20,22] have indicated that there is considerable movement of the lateral pharyngeal walls toward the midline during speech. These movements are somewhat difficult to observe radiographically because of the superimposition of structures in radiographs.[32] Detailed x-ray data regarding medial movement of the lateral pharyngeal walls were reported by Iglesias et al.[4] They obtained simultaneous lateral still radiographs and frontal tomograms in 25 young adults. Lateral and posterior pharyngeal wall displacements were measured for the four vowels /i,u,a,ae/ and the two consonants /z/ and /n/. The medial displacement at the palatal plane was found to be least for the one nasal sound /n/. In our study, we used the nasal "ng" sound and the findings were in agreement with those of Iglesias et al. Little posterior pharyngeal movement was noted compared to the lateral wall displacement. Iglesias et al found that lateral pharyngeal wall movement varied in relation to the speech sound produced. Greater lateral pharyngeal wall displacement occurred for the nonnasal speech sounds than for the nasal /n/, and most of it occurred at or just below the palatal plane.

In our study in which the nasal "ng" sound was used, considerable movement of the lateral pharyngeal wall could be observed, such that at the highest frequencies in some subjects the pharyngeal walls appeared to "wrap themselves" around the aryepiglottic rim; and at the highest frequencies they often covered it, as shown in Fig 3E. There was far more movement in the lateral than in the posterior pharyngeal walls.

One would suspect that extrinsic laryngeal muscles would be involved to effect the difference in height as well as the difference in lateral pharyngeal wall movement. In the study by Honda and Estill,[18] electromyographic data were recorded from extrinsic muscles over a two-octave range (196 to 784 Hz). In all qualities at 784 Hz, these muscles were most active; this finding suggests that the consequence of extrinsic muscle activity might be a higher larynx and a narrower vocal tract configuration than were observed in the present study.

SOFT PALATE ACTIVITY

One of the striking features of this study concerns the lifting of the soft palate and the uvular muscle and the narrowing of the velopharyngeal port with increase in F0. The use of the nasal sound "ng" allowed us to observe the elevation of the soft palate with rising pitch. At the highest frequencies, the velopharyngeal port opening was obliterated and the "ng" sound was lost. This supports the subjective sensations reported by Lehmann in 1902[46] and the video documentation of Brewer et al in 1974.[36] Lehmann felt that as the scale ascended, the sensation in the palate moved posteriorly, until at the highest frequencies (above 1,047 Hz) the uvula itself was lifted. Brewer et al,[36] with the fiberscope on the floor of the nasal fossa, recorded that as frequency was raised, more and more of the posterior portion of the soft palate lifted as well. In more anterior positioning of the fiberscope by Brewer et al, the lumen of the velar port was not open to view.

It is generally agreed that the velum is elevated and retracted by means of the levator veli palatini muscle. The manner of velopharyngeal closure has been studied by many investigators.[1-18,20,23-25,27,29-32,47,48] Niimi et al[17] have suggested that besides the sphincteric and "trapdoor" mechanisms for closure, there may be a mixture of the two, with the contribution of each differing among speakers. In the current study, it appears that whether one type of action or the other occurs may depend on voice quality in the same speaker. In Fig 7, one might argue that the velopharyngeal port closure is slightly more closed in sob and falsetto qualities, while in speech and opera, there is a wider distance between the posterior pharyngeal wall and the rising uvular muscle. Thus, velopharyngeal port closure in falsetto and sob might be classed as more sphincteric, while in speech and opera, it may be of the "trapdoor" variety.

TILTING OF THYROID CARTILAGE

The larynx appeared to tilt anteriorly at higher frequencies (Fig 7C,F,L). This is not a new observation, having been noted by many investigators.[8,16,22-25] Contraction of the pharyngeal constrictors could well result in a dorsocranial pull, lifting the thyroid cartilage posteriorly, while contraction of the geniohyoid might result in a more anterior and caudal positioning of the thyroid cartilage resulting in its "tilting."[25]

CONSTRICTION OF PHARYNGEAL WALLS AT LOWEST F0

In Fig 5, it was noted that subjects SG and SK constricted the pharyngeal walls when making the lowest F0. In Fig 6B,E,H,K,N, subjects TC and AB displayed the same phenomenon. The pharyngeal constriction in the lowest F0 has been noted many times before.[18,47-50] Honda hypothesized that the cricopharyngeus on contraction bunches behind the cricoid cartilage, causing the cricoid cartilage to rotate forward and thereby shortening the vocal folds and making the production of these lowest frequencies possible.[50]

SUMMARY

Simultaneous velolaryngeal endoscopic procedures were performed in 10 of 11 subjects to examine the action of the soft palate, the pharyngeal walls, and laryngeal height as F0 was raised and lowered.

For all singers, trained and untrained, laryngeal height could be correlated with increases in F0. Further, it was noted that as F0 was raised, both the lumen of the velopharyngeal port and the pharyngeal walls contracted. As F0 decreased, both the velopharyngeal port and the pharyngeal walls expanded with the lowering of the larynx, until the very lowest pitches, at which in some voices the pharyngeal walls again constricted.

In the comparison of qualities within a single subject, it was noted that at 90% of the range, there appeared to be a tilting of the larynx anteriorly and that a sphincteric or "trapdoor" velopharyngeal closure might be quality-dependent.

The videotaping and recording of these phenomena at discrete pitches of the subject's range made possible the analysis of acoustic changes of the nasal "ng" at 10%, 50%, and 90% of the total range in four common voice qualities.

Simultaneous dual velolaryngeal endoscopy proved to be of great value for the understanding of supraglottic contributions to pitch raising.

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ELECTROSURGERY-INDUCED ENDOTRACHEAL TUBE IGNITION DURING TRACHEOTOMY

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Electrosurgery was the most common source of ignition for operating room fires prior to the advent of lasers. When combined with volatile anesthetic mixtures, electrosurgery has caused ignition of plastic, rubber, paper, enteric gases, and combustible preparation solutions. We report on an intubated patient whose polyvinyl chloride endotracheal tube ignited during a tracheotomy performed with an electrosurgical unit. The oxygen-rich environment, the polyvinyl chloride tube, and the heat generated by the electrosurgical unit combined to produce a fire. Since otolaryngologists are called upon often to perform tracheotomies on intubated patients, it is imperative that they understand the factors involved in the development of such a fire. This case is presented with an explanation of why this type of fire occurs. A brief review of the literature is included. Different kinds of electrosurgical units, precautions as to their use, and the management of electrosurgery-induced endotracheal tube fires are also discussed.

KEY WORDS — cautery, electrocautery, electrosurgery, endotracheal tube, fire, ignition, tracheotomy.

INTRODUCTION

There are three reported cases of electrosurgery-induced endotracheal tube fires.[1-3] We report a fourth case that occurred during elective tracheotomy. In elective tracheotomies the airway may be intubated, and an airway fire can result if electrosurgery is used in close proximity to the endotracheal tube. In this paper we review the different kinds of electrosurgical units, briefly summarize precautions to be implemented during their use, and describe management of artificial airway fires.

CASE REPORT

A 57-year-old woman was involved in a motor vehicle accident as an unrestrained passenger. She sustained multiple system injuries, including a closed head injury, a large scalp laceration, a left pneumothorax, and a fractured pelvis. She was comatose on admission and required endotracheal intubation for airway protection and controlled ventilation. Over the first 10 days of hospitalization there was no neurologic improvement and attempts to wean her from the respirator were unsuccessful. On the 10th day of hospitalization she was taken to the operating room for tracheotomy and gastrostomy.

In the operating room, she was put in the supine position and prepared and draped in the usual fashion for a tracheotomy. A grounding pad was placed on the patient. (Maximum levels for cutting and coagulating were not noted on the operating room record.) A transverse skin incision was made two finger-breadths above the sternal notch. The incision was carried down to the level of the strap muscles and through the midline to the trachea. The thyroid isthmus was not in the operative field at the level of the second to fourth tracheal rings. Electrosurgery was then used to coagulate a vessel overlying the trachea and subsequently to enter the trachea through a vertical incision. One hundred percent oxygen was used to ventilate the patient prior to incising the trachea to maximize the patient's oxygen saturation. This was done in anticipation of the short period of apnea that is usually required to switch from the oral endotracheal tube to the tracheotomy tube. When the trachea was entered an ignition of the endotracheal tube occurred with a small explosion and fire. The oxygen source was immediately disconnected and the endotracheal tube removed. There was no evidence of fire in the airway once the endotracheal tube was removed. The tracheotomy was quickly completed, with the patient showing no evidence of deterioration. Direct laryngoscopy and rigid bronchoscopy were then performed to assess airway damage. Findings on examination of the oral cavity and larynx were within normal limits. The anterior segment of the trachea that surrounded the tracheotomy was charred, but the distal airway was without damage.

Examination of the endotracheal tube revealed the cuff to be perforated and melted. This damage extended 1.5 cm from the endotracheal tube tip. The proximal lumen was full of black char.

The gastrostomy was subsequently performed without incident and the patient was returned to the intensive care unit. She had a chest radiograph performed, which was unchanged from preoperative radiographs. Subsequent daily chest radiographs were also unchanged. The patient died 7 days postoperatively of sepsis unrelated to the endotracheal tube fire.

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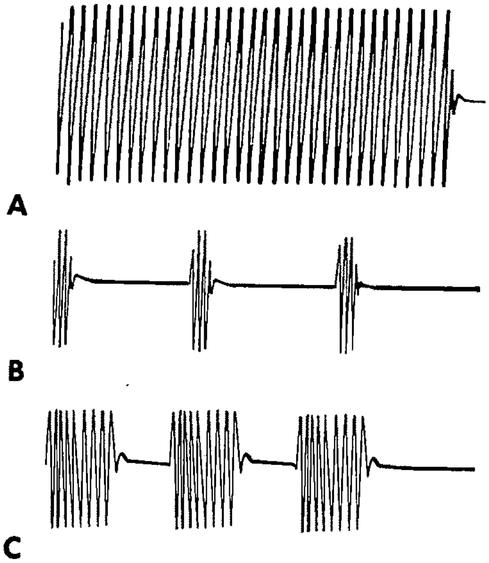

Waveforms produced by monopolar electrosurgical unit. A) Continuous waveform of cutting current. B) Off-on waveform of coagulation current. C) Intermediate waveform that blends cutting and coagulation.

DISCUSSION

Electrosurgery is one of the most commonly used techniques in the operating room. However, historically it has been associated with operating room fires when combined with volatile anesthetic gases. Ignition of substances such as plastic, rubber, paper, enteric gases, and combustible preparation solutions have all been reported.[4]

In most of the medical literature the terms electrocautery and electrosurgery are used interchangeably. However, they have different definitions. Thermocautery is a term used to denote heat that is transferred to the tissues from a preheated object such as a Shaw scalpel or a hot iron. Electrosurgery is a term used to describe coagulation or cutting accomplished by passing high-frequency current through tissue, and it is what most authors refer to when discussing electrocautery or cautery. There are two types of electrosurgical units: monopolar and bipolar. Monopolar units are composed of three basic parts: a generator, an active electrode, and a dispersive electrode or grounding pad. The generator produces a current of electrons that passes through the active electrode in a high-current density fashion, causing destruction of tissue at the tip. The grounding pad collects the current and completes the circuit. Because of its large surface area, the grounding pad reduces the concentration of current as it flows from the patient to the pad, thus preventing electrosurgical effects at the pad's contact point.

Three possible waveforms are produced by a monopolar unit, with each having different effects on tissues.[5] The continuous waveform displayed in the Figure (A) is used to cut tissues. The waveform displayed in the Figure (B) has "off" periods that permit heat dissipation and is used to achieve coagulation. The Figure (C) demonstrates an intermediate-blend mode of operation that is used to both coagulate and cut.

The electrosurgical effects on tissues are due to both the waveform used and the speed at which the current is passed over a volume of tissue. Tissues are vaporized once they reach a temperature of 100°C. Using the cutting mode of an electrosurgical unit to coagulate a specific vessel or bleeding point will impart a greater amount of energy to surrounding tissues than the coagulating or blend modes, because the temperature of vaporization is quickly reached and all extra energy is deposited in surrounding tissues. However, in using the cutting mode to cut tissues by moving the active electrode as one would a scalpel, vaporization occurs but little extra energy is deposited in the surrounding tissues because the electrode moves on to an adjacent volume of tissue.

The reverse is true for the coagulating mode. In coagulating a specific point, less energy is imparted to the tissues because of the "off" times. In cutting tissue with the coagulating mode, the temperature of vaporization is less readily reached than with the cutting mode; thus, the electrode must stay in contact with a particular volume of tissue for a longer time and deposit more energy in the surrounding tissues, leading to more tissue destruction.

Bipolar units are composed of a generator and two electrodes located at either end of a forceps. Electrons flow from one tip of the forceps and are collected by the other to complete the circuit. The electron flow is limited to the ends of the forceps and thus causes minimal surrounding tissue damage — far less than that of any monopolar waveform. Bipolar units have the advantages of 1) coagulating vessels even when the forceps is immersed in blood and 2) limiting damage to surrounding structures. They are not helpful in cutting tissue.

With the addition of our case there are four reported cases of electrosurgery-induced endotracheal tube ignitions. Boyd[1] in 1969 reported an oral fire during the removal of a tonsillar tumor with diathermy. A high diathermy setting excessively heated tissues that then landed on the endotracheal tube and burned through it. This allowed oxygen to flow to the outside of the tube and started a small tube fire. Rita and Seleny[2] in 1982 reported a case in which an endotracheal tube was passed through a tracheotomy for airway control. A urethral resectoscope was then used to remove granulation tissue at the tracheotomy site just superior to the tube. The electrosurgical active electrode presumably perforated the endotracheal tube and it subsequently ignited. In a third case, reported by Simpson and Wolf[3] in 1986, a 4-year-old child was intubated with an uncuffed polyvinyl chloride tube that allowed a small air leak. During the performance of an electrosurgery tonsillectomy, the tube ignited.

In our case, upon incision of the trachea the electrosurgical unit caused a perforation of the endotracheal tube cuff, thus allowing a backflow of oxygen around the tube that caused a fire to occur.

Although endotracheal tube ignition by electrosurgery may be an infrequent complication, it is potentially fatal. An understanding of the mechanism involved in the induction of such fires is essential to the otolaryngologist. In order for combustion to take place, an ignition source (electrosurgery), a carbon source (the endotracheal tube), and oxygen must all be present in close proximity.[3] Studies of laser endotracheal tube fires have shown that increasing the oxygen concentration of the environment in and around the tube decreases the threshold for ignition and supports combustion.[6] A common feature to all the reported cases is an increase of the oxygen concentration in the immediate microenvironment surrounding the tube. This, when coupled with either a spark or high temperatures induced by electrosurgery, may cause the endotracheal tube to ignite.

Certain precautions are helpful in reducing the risk of electrosurgery-induced endotracheal tube fires. When a monopolar unit is used, a grounding pad must be appropriately placed on the patient to prevent inadvertent current flow to undesirable areas such as an endotracheal tube. Because the cutting waveform imparts more power to the tissues, it is more likely to induce an ignition. Whenever one is working around an endotracheal tube and electrosurgery has to be used, a bipolar unit is recommended. As demonstrated by the cases reviewed, it is desirable to reduce the oxygen concentration of the immediate microenvironment of the tubes by ventilating the patient with the lowest practical oxygen concentration. However, it is important to note that certain anesthetic gases such as nitrous oxide support combustion as well as oxygen, and their use should also be minimized. Finally, during tracheotomy of the intubated patient, electrosurgery should not be used as the dissection proceeds close to the trachea.

The prompt, efficient management of an endotracheal tube fire can mean the difference between a minor and a fatal complication. Every surgeon should be well aware of procedures to follow in such an emergency. When an endotracheal tube fire is recognized the surgeon should immediately turn off the electrosurgical unit, and the anesthesiologist should disconnect the oxygen supply and remove the endotracheal tube from the airway. The patient should then be reintubated and rigid bronchoscopy performed. Flexible bronchoscopy is recommended if there is a need to wash out the distal airway and remove products of combustion. Direct laryngoscopy and examination of the oral cavity are also performed. In the immediate postoperative period the patient should have a chest radiograph performed to rule out a pneumothorax. Some patients may require intubation if the original procedure did not involve airway control. Close monitoring for a few days postoperatively in an intensive care setting will help detect possible late respiratory deterioration due to inhalation injury. Endoscopy should be performed frequently in the early postoperative course to assess damage to the trachea and bronchial tree and to remove protein casts that may form. Antibiotics and steroids are recommended to reduce infection and inflammation. If the damage is extensive, positive end expiratory pressure ventilation may be helpful. A Montgomery® Safe-T-Tube can be used for prolonged stenting in cases of extensive tracheal injury.

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LARYNGEAL CHANGES DURING EXERCISE AND EXERCISE-INDUCED ASTHMA

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Exercise-induced asthma is defined as bronchospasm within the distal airways initiated by exercise. Whether the larynx responds to produce an exacerbation or alleviation of symptoms during an attack has never been evaluated. Thirty subjects were tested, including 15 normals and 15 with exercise-induced asthma. Laryngeal response to exercise was determined by measuring the area of the glottic aperture before, during, and after exercise. The glottis was visualized with a flexible laryngoscope and video images were recorded during monitoring of respirations. Asthma was induced in subjects by having them exercise on an ergometer for 10 minutes while breathing dry air at 10°C. Measurements were subsequently made from recorded images and relative glottic areas were compared between groups. Our data quantify the normal physiologic response of the larynx to exercise and demonstrate a substantial laryngeal contribution to asthma induced by exercise.

KEY WORDS — exercise-induced asthma, exercise physiology, laryngeal physiology.

INTRODUCTION

In 1885 Hooper[1] first reported observing movements of the vocal cords during respiration, noting movement apart during inspiration and approximation during expiration. Since this simple beginning our understanding of the physiology of the larynx has been advanced considerably. One area that has not been specifically investigated is the response of the larynx to the stress of extreme exercise. Observational reports have been published,[2] but a quantitative study of the laryngeal response has not been done.

Exercise-induced asthma is defined as acute bronchospasm following the respiratory stress of exercise. During exercise, in which minute ventilation may increase 30 times over resting values, the airways are cooled by the rapid inspiration of cold air combined with evaporation of water vapor from respiratory epithelium.[3] The surface osmolarity of the airways also increases owing to evaporation leading to mast cell sensitivity.[3,4] Following exercise rapid rewarming of the airways leads to degranulation of sensitized mast cells, producing acute bronchospasm, localized edema, and the manifestations of asthma.[4,5] Exercise-induced asthma is highly prevalent, affecting 80% of all asthmatics in general.[6] Studies of Olympic athletes show that 12% of highly trained athletes exhibit asthma that is inducible by exercise.[6,7]

The laryngeal response during an asthmatic episode has been previously studied.[8-11] Narrowing at the glottis has been observed, and increased laryngeal resistances have been measured during asthma induced by methacholine or histamine or during spontaneous attacks.[10] The larynx, however, has not been evaluated during asthma induced by exercise.

Our study was designed to quantify normal changes occurring at the glottic aperture during exercise in normal subjects. Changes measured in asthmatic subjects during exercise are compared to determine if a laryngeal contribution exists to asthma induced by exercise.

MATERIALS AND METHODS

Thirty subjects were studied, with an age range of 18 to 35 years, consisting of 15 normal subjects without a history of respiratory compromise during exercise and 15 with asthma induced exclusively by exercise. Asthmatic subjects had a history of reproducible asthma during exercise responsive to conventional medications. All antiasthmatic medications were discontinued 1 week prior to the study.

Phase 1 (Rest). Subjects first underwent pulmonary function tests using a pneumotach spirometer (Jager Pneumoscope Spectrum LX-80) to obtain baseline forced expiratory volume in 1 second (FEV1) and forced vital capacity (FVC) prior to testing. Nasal mucosa was anesthetized with 2% tetracaine hydrochloride. Laryngoscopy was performed during rest by means of an Olympus ENF-P2 flexible laryngoscope, and laryngeal images were recorded for 10 respiratory cycles with a low light sensitivity camera (JVC TK-U850U, Olympus 56614 adapter) and video recorder (Toshiba SR-1000). A marker was applied to the endoscope at the nasal outlet so the endoscope position could be reproduced in subsequent endoscopies. Subjects breathed through the spirometer during all endoscopies to record respiratory phase for later correlation with laryngeal images.

Phase 2 (Exercise). Subjects were exercised on an ergometer (Cateye Ergociser) at 75% to 85% of

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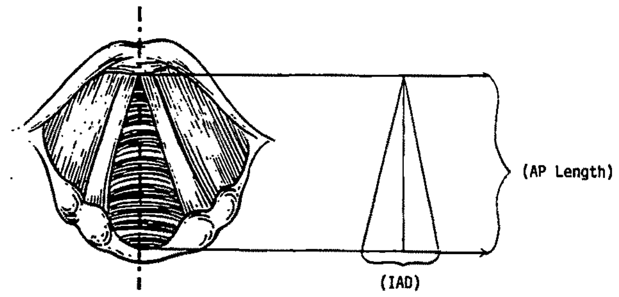

Fig 1. Measurements of glottic aperture were made from video screen image frozen in midinspiration or midexpiration. AP Length — anterior to posterior commissure distance, IAD — interarytenoid distance.

their predicted maximal heart rate (maximal heart rate equals 220 minus subject's age[12]) for 8 minutes while breathing dry air at 10°C.[13,14] Laryngoscopy was repeated during exercise at an elapsed time of 8 minutes, again with recording of 10 respiratory cycles.

Phase 3 (Recovery). Exercise was discontinued and the subject breathed room air during recovery. At 5 minutes laryngoscopy was repeated. Final pulmonary function tests were done to determine the degree of respiratory obstruction produced.

Measurements were subsequently made from the video monitor with the laryngeal image frozen in either midinspiration or midexpiration. Measurements were made of the anteroposterior glottic dimension and interarytenoid distance (Fig 1). For each phase of study, 10 measured values were averaged for each subject. Magnification error possibly introduced between phases if the endoscope tip-to-glottis distance varied (Fig 2) was corrected by treating the anteroposterior glottic dimension as a constant. This allowed for adjustment of phase 2 and 3 measurements to the phase 1 standard.[8,15] The area at the glottic aperture was then calculated by treating it as an isosceles triangle (Fig 1) and using corrected dimension values for area determinations.

Differences in absolute laryngeal size made direct comparison of measurements between subjects impossible. Thus, nondimensional area ratios were calculated to allow for data comparisons (Table 1). Statistical analysis used Student's *t* test.

RESULTS

Subjects were divided into five groups based on induction response. Group A consisted of 13 normal subjects who developed no change in FEV1 or FVC after exercise. Group B consisted of 2 normal subjects who developed a drop in FEV1 or FVC of greater than 5%. Group C contained 7 asthmatics exhibiting minimal induction, with FEV1 or FVC decreasing by less than 5%. Group D included 6 asthmatics with induced drops of FEV1 or FVC by 5% to 15%, while group E contained 2 asthmatics with induced drops of FEV1 or FVC by greater than 15%.

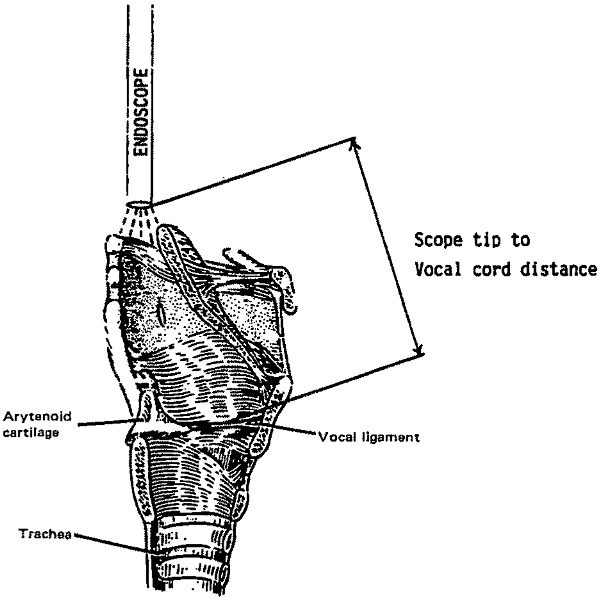

Fig 2. Variation in endoscopic distance produced inconsistent magnification of glottic image. Intrasubject variation between phases was adjusted by holding anteroposterior glottic dimension as constant allowing for determination of correction factor.

The seven calculated ratios for the five subject groups are given in Table 2. Comparisons of data between normal subjects, moderately induced asthmatics, and strongly induced asthmatics in groups A, D, and E, respectively, are shown in Figs 3 and 4. (Ratios are converted to percentages for the sake of clarity.) Statistical analysis compares group D and E results to those of group A (Table 2).

During rest the three subject groups showed a similar degree of vocal cord closure on expiration, with relative areas of 60%, 67%, and 74% of the inspiratory area, respectively. The minor variation between groups was insignificant (Fig 3A).

During exercise and postexercise phases, expiratory laryngeal areas in group A (normal subjects) increased as expected to 86% and 81% of the inspiratory area, respectively. In group D (moderate asth-

TABLE 1. COMPARATIVE RATIOS

Ratio	*Utility*
Resting MEGA/resting MIGA	Resting laryngeal variation
Exercise MEGA/exercise MIGA	Exercise laryngeal variation
Postexercise MEGA/ postexercise MIGA	Laryngeal variation during recovery
Exercise MIGA/resting MIGA	Inspiratory glottic dilation produced by exercise
Postexercise MIGA/resting MIGA	Inspiratory glottic dilation present during recovery
Exercise MEGA/resting MEGA	Expiratory glottic dilation produced by exercise
Postexercise MEGA/resting MEGA	Expiratory glottic dilation present during recovery

MEGA — midexpiratory glottic area, MIGA — midinspiratory glottic area.

TABLE 2. CALCULATED GROUP RATIOS

	Subject Groups				
	A	*B*	*C*	*D*	*E*
Resting laryngeal variation	0.60	0.70	0.68	0.67	0.74
Exercise laryngeal variation	0.86	0.85	0.77	0.63*	0.42†
Postexercise laryngeal variation	0.81	0.67	0.84	0.67*	0.42†
Inspiratory dilation with exercise	1.13	0.83	1.03	1.06	0.85
Inspiratory dilation postexercise	1.06	1.03	1.02	1.06	1.25
Expiratory dilation with exercise	1.74	1.01	1.20	1.06*	0.49†
Expiratory dilation postexercise	1.48	0.98	1.27	1.07*	0.74†

*Significant difference at 1% probability level when compared to group A normals.

†Significant difference at 5% probability level when compared to group A normals.

matics) expiratory areas were similar to the resting expiratory areas at 63% and 67% ($p > .01$) despite a marked increase in minute ventilation. Expiratory areas in group E (severe asthmatics) actually contracted to 42% ($p > .05$) for both exercise and postexercise phases (Fig 3B).

Inspiratory glottic areas during exercise and recovery had insignificant changes for groups A and D (normal subjects and moderate asthmatics) when compared to rest. Inspiratory changes in group E (severe asthmatics) were inconsistent (Fig 4A).

Glottic areas during expiration showed substantial differences among the three groups. In group A (normals), expiratory areas dilated to 174% and 148% of the resting area during exercise and postexercise phases. In group D (asthmatics) there was effectively no dilation, with areas of 106% and 107% of the resting area ($p > .01$). Group E (severe asthmatics) actually exhibited laryngeal contracture, with areas deceasing to 49% and 74% of the resting area during exercise and postexercise phases ($p > .05$) (Fig 4B).

Group C (uninduced asthmatics) produced ratios very similar to those of group A (normal subjects), while group B (induced normals) gave values closest to those of group D (moderate asthmatics) (Table 2).

DISCUSSION

Our study identifies a decrease in respiratory variation and expiratory glottic closure during exercise and the postexercise state in normal subjects, while in asthmatics this natural accommodation did not occur. Baier[16] discusses the effect of varying the glottic aperture on laryngeal resistance to airflow. By modifying Rohrer's original equation to the form $Rua = (k1' + k2'Vao)/A^2$ (where Rua = glottic resistance, Vao = airflow, A = glottic area, and k1' and k2' are modified Rohrer's constants that are based on a triangular glottic shape and turbulent airflow) Baier calculated laryngeal resistance for various airflows and glottic areas.

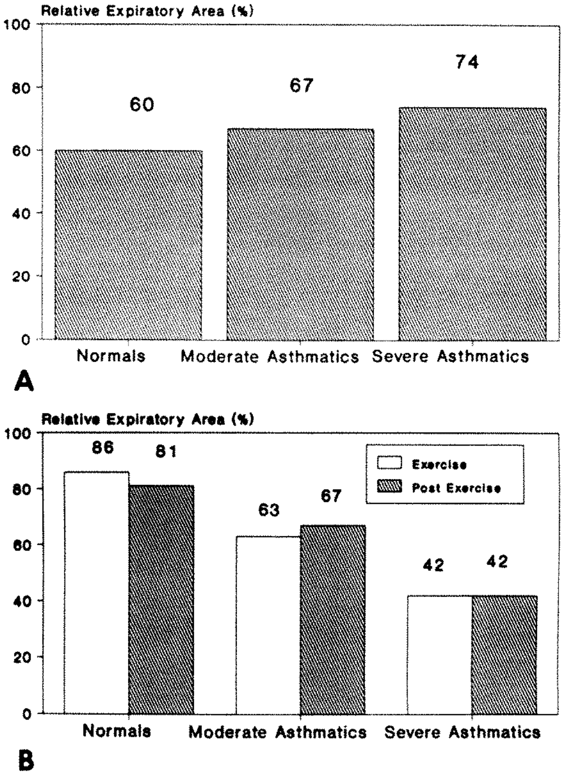

Fig 3. Laryngeal variation. A) Resting. Midexpiratory glottic areas shown as percentage of midinspiratory glottic area during quiet ventilation. B) During exercise and postexercise. Midexpiratory glottic areas shown as percentage of phase equivalent midinspiratory glottic area during exercise and recovery.

Ferris[17] found that the upper airways contribute 46% of the total pulmonary resistance during mouth breathing (at a flow of 1 L/s), with the larynx contributing 26% of the total. During exercise, airflow through the airways increases substantially, leading to increased turbulence in the upper airways. As flow increases, the resistance in a turbulent flow system increases faster than that in a laminar flow system (lower airways). Thus, the upper airway fractional contribution to total pulmonary resistance would be expected to increase in higher flow states. This effect is partially counteracted by laryngeal accommodation through dilation, allowing the resistance of the upper airways to remain essentially constant during exercise.[18] In our study, the expiratory glottic area in normal subjects increased by 74% during exercise. According to Baier's equation this would lead to a net decrease of 67% in laryngeal resistance at any given flow.

Our study shows that in patients with exercise-induced asthma this accommodation does not occur; hence, there is increased laryngeal resistance from higher flows and stationary or smaller glottic apertures. This effect increases both upper airway resistance and total pulmonary resistance during exercise, thus increasing the required work of respiration. An asthmatic athlete's performance may be further limited under these conditions.

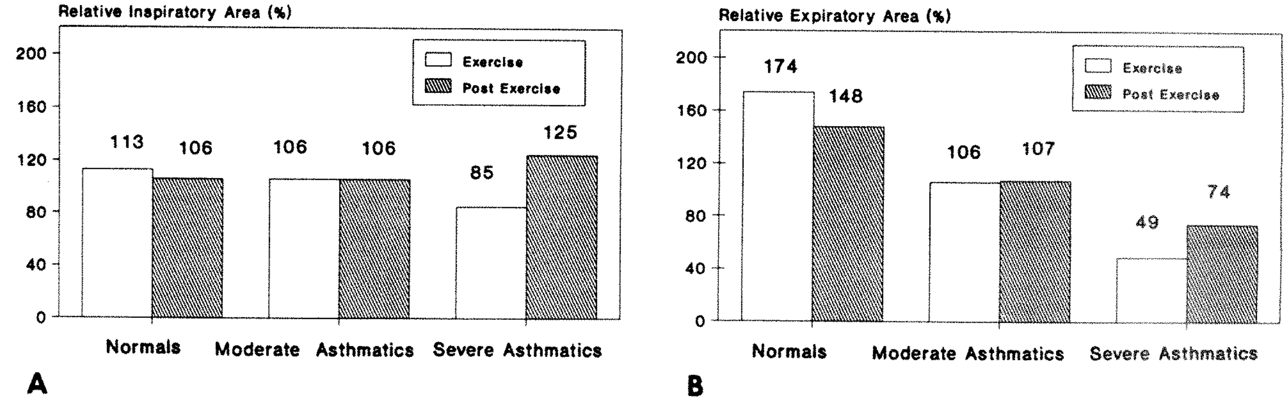

Fig 4. Laryngeal dilation during exercise and postexercise. A) Inspiratory. Exercise and recovery midinspiratory glottic areas shown as percentage of resting midinspiratory glottic area. B) Expiratory. Exercise and recovery midexpiratory glottic areas shown as percentage of resting midexpiratory glottic area.

England[8] has shown similar closures of the glottis during expiration in spontaneous asthma and asthma induced by drug challenge. Collett,[9] by applying constant positive airway pressure to subjects, was able to reverse the increased laryngeal resistance during an asthmatic attack. Laryngeal closure occurring during exercise-induced asthma may be viewed as an endogenous source of continuous positive airway pressure that aids in keeping distal airways open, thereby lessening the severity and progression of the asthmatic attack.

CONCLUSIONS

1. Inspiratory glottic areas do not change during exercise or recovery in either normal or asthmatic subjects.
2. Expiratory glottic areas increase substantially during exercise and recovery in normal subjects but do not change or in fact decrease in asthmatics.
3. Respiratory laryngeal variation in normal subjects decreases during exercise and recovery, while in asthmatics it either does not change or increases.
4. A relative narrowing of the glottis does contribute to airway obstruction in patients with exercise-induced asthma, but may act to limit the progression and severity of an attack.

ACKNOWLEDGMENTS — Special thanks to Olympus Instruments (Lombard, Ill) and the Department of Respiratory Therapy (Frank Haas) for equipment donations.

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CONTEMPORARY MANAGEMENT OF NEUROFIBROMATOSIS

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The neurofibromatoses are two distinct entities with different genetic origins. The phenotypic expressions and required treatments are different. The devastating nature of neurofibromatosis-2 may be more effectively controlled through the application of advanced imaging techniques and contemporary neurotologic procedures. The most common manifestation of neurofibromatosis-2 is that of bilateral acoustic neuromas. The eventual total bilateral sensorineural deafness associated with this condition can be obviated in selected cases if the diagnosis is established early. Follow-up data are reported for three patients in whom hearing was preserved in at least one ear. When removal with hearing preservation is not possible, subtotal tumor removal with decompression of the internal auditory canals may delay progression of hearing loss. A new approach to tumors of the pterygomaxillary fossa that have extended to the middle cranial fossa has been successfully applied and is described.

KEY WORDS — acoustic neuroma, genetic disorders, neurofibromatosis, von Recklinghausen's disease.

The neurofibromatoses are two genetically distinct disorders inherited in an autosomal dominant fashion with high penetrance. The genes for these disorders have recently been located on separate chromosomes. These disorders primarily affect cell growth of neural tissues and can cause tumors to grow on nerves at any time and at any location. A wide range of expressivity is seen even within a family. Resultant manifestations may be innocuous or progressive and may result in significant morbidity or mortality.

The phenotypic or clinical expressions of the neurofibromatoses are different and have been separated into a two-category classification.[1] The most common type, neurofibromatosis-1 or NF-1 (previously known as von Recklinghausen's neurofibromatosis or peripheral neurofibromatosis) affects approximately 100,000 people in the United States. Neurofibromatosis-1 is considered present when two or more of the following diagnostic criteria are found.

1. Six or more café au lait macules over 5 mm in greatest diameter in prepubertal individuals and over 15 mm in greatest diameter in postpubertal individuals.
2. Two or more neurofibromas of any type or one plexiform neurofibroma.
3. Freckling in the axillary or inguinal regions.
4. Optic glioma.
5. Two or more Lisch nodules (iris hamartomas).
6. A distinctive osseous lesion such as sphenoid dysplasia or thinning of long bone cortex, with or without pseudoarthrosis.
7. A first-degree relative (parent, sibling, or offspring) with NF-1 by the above criteria.

Neurofibromatosis-2 (NF-2 or bilateral acoustic neurofibromatosis) affects several thousand Americans. The criteria for NF-2 are met by an individual who has 1) bilateral eighth nerve masses seen with appropriate imaging techniques (eg, computed tomography [CT] or magnetic resonance imaging [MRI]) or 2) a first-degree relative with NF-2 and either a unilateral eighth nerve mass or two of the following: neurofibroma, meningioma, glioma, schwannoma, or juvenile posterior subcapsular lenticular opacity.

Neurofibromatosis-1 must be distinguished from NF-2 because of substantive differences in the natural history, prognosis, and required treatment. This differentiation can be made by identification of the varied phenotypic expressions. The age at onset of symptoms and signs may also provide valuable insights as to the neurofibromatosis type. Neurofibromatosis-1 is often diagnosed at birth or during infancy and almost always during the first decade by examination of the skin. In contrast, NF-2 does not generally become clinically apparent until puberty or early adulthood, and may appear as late as the seventh decade of life.[2]

Both forms of neurofibromatosis are often accompanied by distinct eye changes that can be definitive in diagnosis. Lisch nodules of the iris occur in more than 85% of postpubertal patients with NF-1, but have not been seen in patients with NF-2. Posterior capsular opacities of the lens are seen in most patients with NF-2 by age 30, but have not been described in patients with NF-1.[3] Optic gliomas, while seen in NF-1, are not seen in patients with NF-2.

BIOLOGIC AND MOLECULAR GENETIC STUDIES

Two clinical observations suggest that a growth

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or hormone factor may contribute to tumor formation in both NF-1 and NF-2. First, skin neurofibromas usually do not appear until puberty,[4] and the acoustic neuromas of NF-2 commonly become symptomatic during or soon after puberty.[5] Second, pregnancy can affect the tumors in both forms of the disorder.[6]

The gene for NF-1 was recently mapped to chromosome 17 by linkage analysis.[7] The location of the gene for NF-2 was first suggested by Seizinger et al[8] in a study of chromosomal markers in tissue from human acoustic neuromas. Using a molecular genetic approach, these investigators demonstrated that acoustic neuroma is associated with loss of genes on chromosome 22. They proposed that tumor growth occurred by a mechanism of tumorigenesis that had been discovered in embryonal tumors with recombinant DNA techniques. By this mechanism, the formation of a tumor is a two-step process. The initial event is a primary mutation resulting in the formation of an allele that is recessive at the cellular level to the normal allele. The growth of a tumor occurs only after an additional change such as a loss of a chromosome or mitotic recombination eliminates the normal allele, thus unmasking the altered allele. The primary mutation may be transmitted in the germline, thus resulting in a familial disease. Seizinger et al[8] also suggested that a common molecular event underlies the formation of acoustic neuromas and meningiomas. Patients with NF-2 frequently develop meningiomas, and the association of meningiomas with loss of genes on chromosome 22 has been reported in cytogenic studies of cultured meningiomas.[9]

In a subsequent study, Seizinger et al[10] demonstrated specific loss of alleles from chromosome 22 in two acoustic neuromas, two neurofibromas, and one meningioma from patients with NF-2. The two neurofibromas were taken from the same patient, and both showed loss of identical alleles demonstrating that the same chromosome suffered deletion in both tumors. Only a portion of the long arm of chromosome 22 was deleted in the two acoustic neuromas, narrowing the possible chromosomal location of the gene that causes NF-2 to the region distal to the D22S9 locus in band 22q11. The future identification of progressively smaller deletions on chromosome 22 in these tumor types may well provide a means to further characterize the defect in this disorder.[10]

By linkage analysis of a large kindred with NF-2, Rouleau et al[11] confirmed that the inherited genetic abnormality for NF-2 is on the long arm of chromosome 22.

Wertelecki et al[12] studied 15 males and 8 females of one large kindred with NF-2. Between the ages of 15 and 53 years, the patients had multiple central nervous system tumors of various types, but most notably, bilateral acoustic neuromas. Two or more tumors eventually developed in 20 of the patients; 9 had evidence of only bilateral acoustic neuromas. The analysis of D22S1 and IGLV DNA markers for coinheritance with NF-2 indicated that the locus for the disorder is near the center of the long arm of chromosome 22 (22q11.1–22q13.1).

The presence of posterior capsular cataracts in a young individual at risk for NF-2 is highly suggestive of this disorder.[5] It is significant that one of the genes controlling beta-B2 lens crystallin is also on chromosome 22.[13]

An interdisciplinary team has been established to assess and treat neurofibromatosis patients at the Indiana University Medical Center. More than 200 patients are now enrolled in the program. We selected several patients with head and neck manifestations of neurofibromatosis to illustrate current management concepts.

CASE REPORTS

Patient 1. A 10-year-old boy with multiple café au lait spots presented with a large mass of the left parotid compartment that compressed and occluded the ear canal, leading to a maximum conductive hearing loss. A biopsy of a retroauricular extension of this mass yielded a histopathologic diagnosis of plexiform neurofibroma. Because of risk to the facial nerve posed by surgical removal, the mass is currently being followed and the occluded ear canal has been managed by an open ear mold.

Comment. The known proclivity of plexiform neurofibromas to entwine themselves in and around nerve fibers would place the facial nerve at considerable risk with any attempt at complete removal of this tumor. Care must be exercised so as not to create a neurologic deficit that would be more debilitating than the lesion under treatment. A simple solution (open ear mold) to the occluded ear canal seems most appropriate at this time.

Patient 2. A 26-year-old man with known neurofibromatosis presented with proptosis of the left eye. Computed tomography demonstrated bilateral tumors of the pterygomaxillary fossae with extension into the middle cranial fossae (Fig 1). The tumors were sequentially removed through a combined middle fossa and transmaxillary approach (Fig 2). The middle fossa extension was removed through a temporal craniotomy. The pterygomaxillary fossa was then approached transantrally. The anterior wall of the maxillary sinus was removed via a Caldwell-Luc approach. The posterior wall of the maxillary sinus was then removed and the tumor was accessed. The tumor was then pushed inferiorly from above and extracted through the maxillary sinus.

Patient 3. A 31-year-old woman presented with

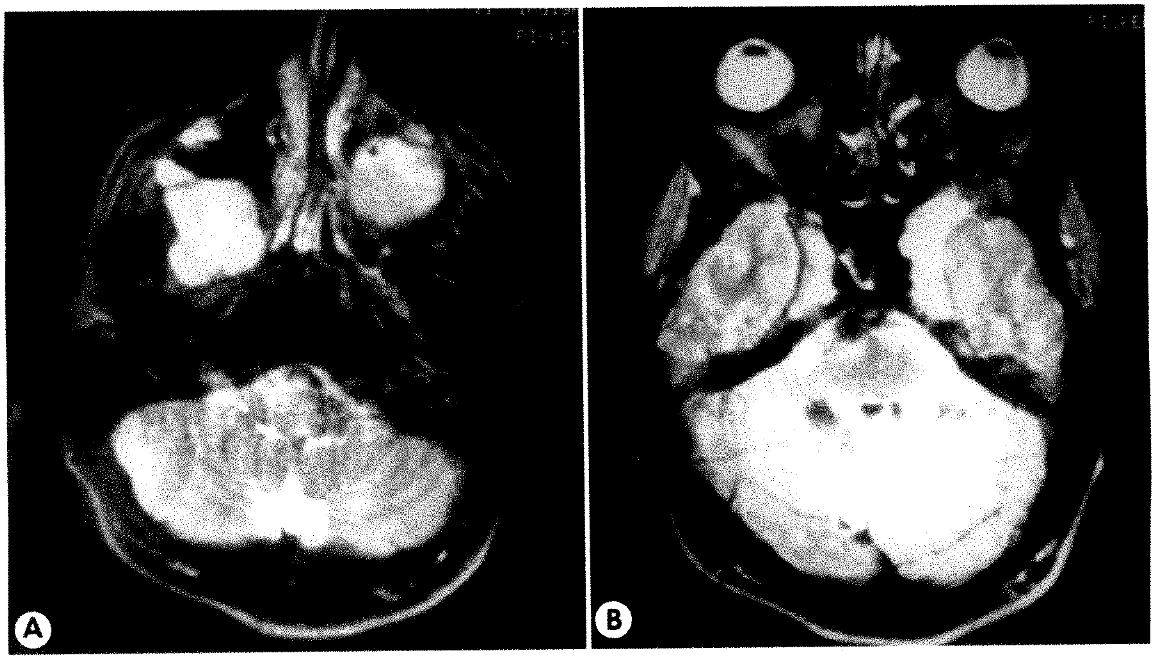

Fig 1. (Patient 2) Computed tomography demonstrating A) bilateral tumors of pterygomaxillary fossae and B) extension of tumors into middle cranial fossae.

severe headaches, ataxia, and bilateral hearing loss. The diagnosis of bilateral acoustic tumors had been made 7 years previously, but no treatment was initially administered. An audiogram demonstrated a 45-dB sensorineural hearing loss (pure tone average [PTA]) with 92% discrimination on the left and an 80-dB sensorineural loss with 0% discrimination on the right. Computed tomography demonstrated large bilateral acoustic neuromas and evidence of hydrocephalus (Fig 3). On December 18, 1987, a bilateral subtotal removal of the acoustic neuromas was performed at the same sitting, and the left internal auditory canal was decompressed. The patient's hearing remained relatively stable for 2 years, but she has recently noted some progression of the loss in the left ear, primarily affecting the low frequencies. The PTA is 80 dB with 68% discrimination.

Patient 4. A 28-year-old man with NF-2 associated with bilateral acoustic neuromas and multiple intracranial meningiomas experienced a gradually progressive hearing loss that resulted in total deafness. He has undergone several subtotal removals of his acoustic neuromas and has participated in clinical trials of various vibrotactile devices since 1982. Benefits have been primarily in the detection of suprasegmental features of speech. His performance in a laboratory setting is similar to that seen in single-channel cochlear implant subjects.[14]

HEARING PRESERVATION CASES

We have previously reported our experience with attempts at hearing preservation in patients with NF-2.[15] Included herein are updated status reports on three patients.

Patient 5. An 11-year-old boy was found to have bilateral acoustic neuromas during evaluation of a right-sided hearing loss that had been present as long as he could remember. A large right acoustic neuroma was removed on October 24, 1986 (nonhearing ear). On May 8, 1987, total removal of the left acoustic neuroma was accomplished through a suboccipital-transmeatal approach. An audiogram 4 days postoperatively demonstrated a 10-dB bone conduction level with a 30-dB air conduction level. (A middle ear effusion was present.) His speech discrimination was 96%. Unfortunately, 2 weeks postoperatively the patient developed a sudden sensorineural hearing loss with a PTA of 78 dB and 0% discrimination. Hearing returned to 46 dB with 100% discrimination following a course of prednisone therapy. A 3-year postoperative audiogram demonstrated a 70-dB PTA with 88% discrimination. An aided audiogram demonstrated a 25-dB PTA with 92% discrimination. Follow-up CT demonstrates no evidence of tumor on either side.

Patient 6. A 14-year-old girl presented with a right-sided hearing loss of 2 months' duration. A left hypoglossal nerve neuroma had been removed 4 years previously. Cranial nerve examination demonstrated paralysis of the left cranial nerves X, XI, and XII. An audiogram demonstrated a 20-dB PTA with 100% discrimination on the left and a 60-dB PTA with 54% discrimination on the right. Computed tomography demonstrated bilateral expansion of the internal auditory canals, and MRI demonstrated bilateral acoustic neuromas. The tumor on the right was intracanalicular, and the one on the left protruded 1.5 cm medial to the porus acusticus.

Total removal of the left acoustic neuroma (bet-

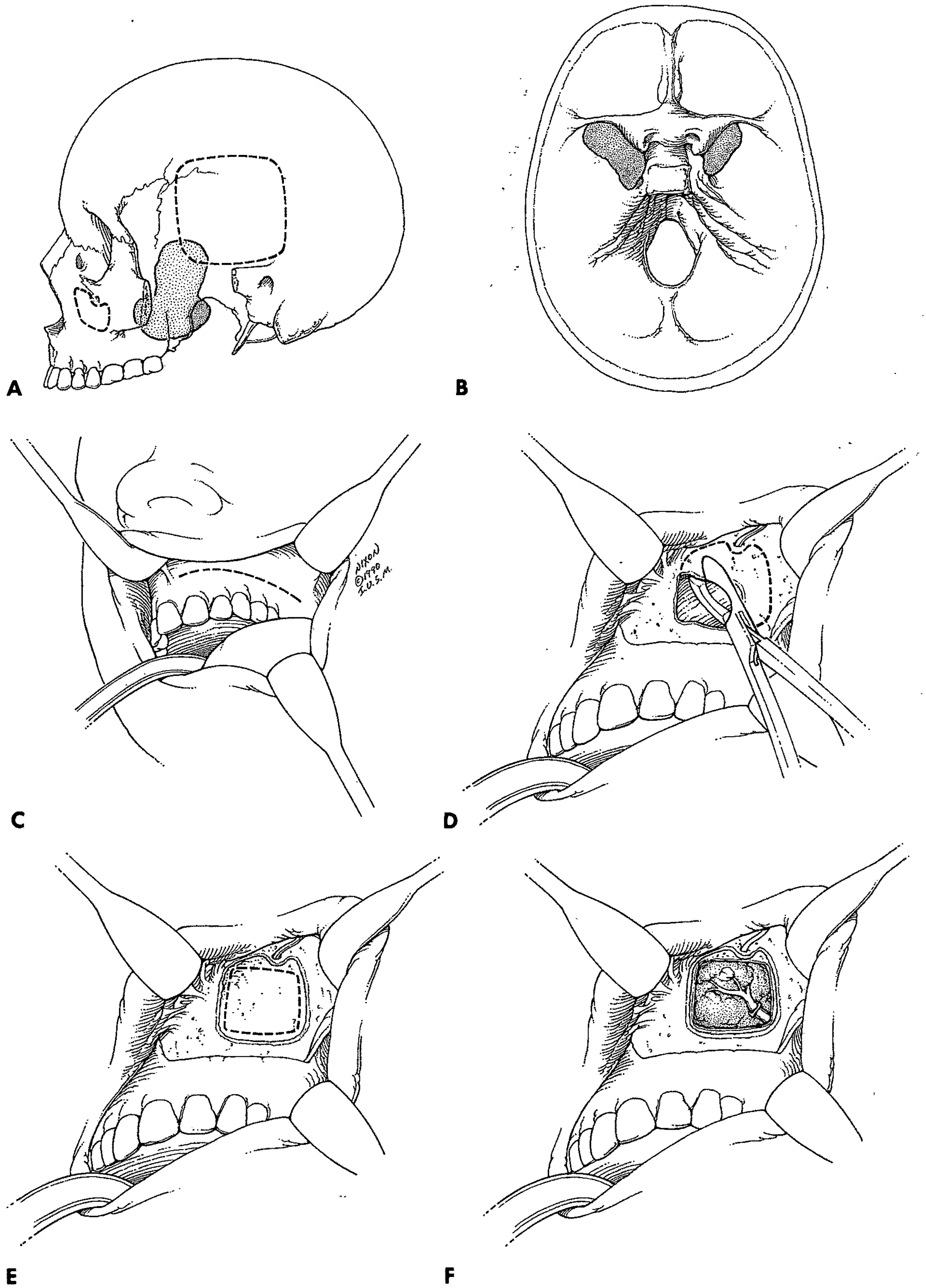

Fig 2. (Patient 2) Representation of removal of tumors. A) Combined middle fossa and transmaxillary approach. B) Portions of tumors accessed through middle fossa approaches. C) Sublabial incision. D) Window created in anterior face of maxilla. E) Window created in posterior wall of maxillary sinus. F) Tumor visualized in pterygomaxillary fossa. Excision was performed through this exposure.

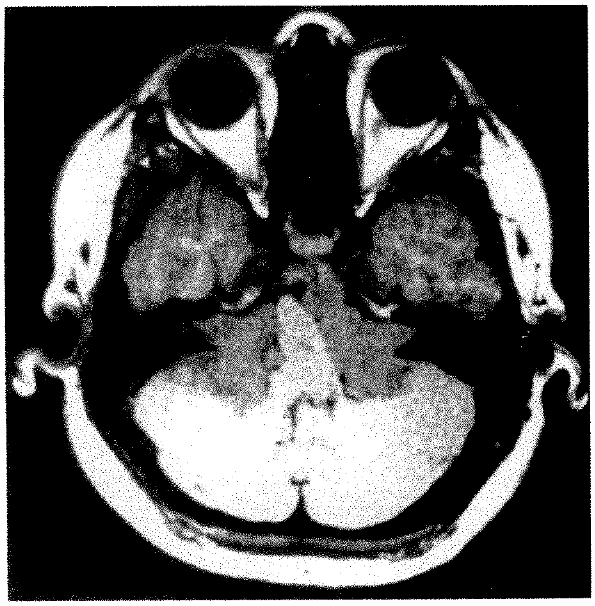

Fig 3. (Patient 3) Bilateral acoustic neuromas.

ter-hearing ear) was accomplished on August 27, 1987, by the suboccipital-transmeatal approach. The right acoustic neuroma was removed on April 19, 1988. Preservation of the facial and cochlear nerves was accomplished bilaterally. A postoperative audiogram 19 months following the removal of the left tumor and 11 months following removal of the right tumor demonstrated a 38-dB PTA with 96% discrimination on the left and a 65-dB PTA with 28% discrimination on the right. An audiogram 2½ years following removal of the left acoustic neuroma demonstrated stability of hearing in the left ear and further deterioration on the right. Magnetic resonance imaging demonstrated no evidence of recurrent tumor.

Patient 7. A 39-year-old woman presented with hearing loss, headache, and a staggering gait. An audiogram demonstrated no responses on the left and a 10-dB PTA with 100% discrimination on the right. Computed tomography revealed multiple frontal meningiomas, a 3- to 4-cm left cerebellopontine angle tumor, and what appeared to be a 1.5-cm right cerebellopontine angle tumor.

On April 15, 1980, a frontal craniotomy was performed and multiple anterior cranial fossa meningiomas were removed. On September 29, 1983, a 3- to 4-cm left acoustic neuroma was removed through a suboccipital approach. Cranial nerves VII and VIII could not be preserved. On December 6, 1984, the right internal auditory canal was approached through a suboccipital-transmeatal exposure. The auditory brain stem response was monitored intraoperatively and the cochlear and facial nerves were preserved. Two small tumors that proved to be meningiomas were totally removed. An audiogram 3 months postoperatively demonstrated a 20-dB PTA with 100% discrimination. Hearing has remained stable in the right ear, and an audiogram performed 6½ years postoperatively demonstrated a 25-dB PTA with 96% discrimination.

DISCUSSION

Individualized treatment plans must be developed for patients with neurofibromatosis because of the wide variability of the clinical presentation and course. The delineation of two phenotypically distinct patterns that have an underlying genetic difference has significantly altered treatment strategies. A patient who clearly falls into the NF-1 group is not at risk of developing bilateral acoustic neuromas. On the other hand, if any finding suggests the diagnosis of NF-2, MRI with gadolinium should be performed to screen for acoustic neuromas or other intracranial tumors. Any patient below the age of 30 who develops an acoustic tumor must be carefully screened for the possibility of an undetected NF-2 condition.

Symptomatic neurofibromas are treated by excision with preservation of function when feasible. Great care is exercised so as not to create a new neurologic deficit that may be more disabling than the neurofibroma under treatment. When lesions occur in nonthreatening locations, observation with no active treatment may be most appropriate.

New approaches to the skull base have rendered treatable lesions that were previously inaccessible. An interdisciplinary approach has created innovative cooperative efforts.

The growth pattern of acoustic neuromas in patients with NF-2 is unpredictable. One or both tumors may progress rapidly and relentlessly and lead to deafness, cerebellar ataxia, visual disturbances, and eventually death secondary to brain stem compression. More commonly, growth is slowly progressive over many years and leads to few limitations until the tumors are large. Magnetic resonance imaging with gadolinium has made it possible to diagnose tumors early and to follow the growth pattern of individual tumors.

Surgical intervention is currently the only definitive treatment for enlarging acoustic tumors. As a general rule, acoustic tumors of any size should be removed when aidable hearing is not present and the patient is suitable for an elective operation. With the identification of genetic markers, improved diagnostic capabilities with use of modern audiometrics and auditory evoked potential testing, and improved imaging techniques with use of MRI with gadolinium, diagnosis at an early stage when hearing preservation is feasible will be made more frequently.

Since acoustic tumors arise from the vestibular nerves, surgical removal with preservation of the facial nerve and cochlear nerve and their blood supply is possible. However, the tumor biology is highly variable and even small tumors may be invasive early in their course. Although this tendency to invade cannot be predicted by preoperative imaging studies, the relationship of the tumor to the cochlear nerve can be determined during surgical exploration of the internal auditory canal. With improved surgical techniques and intraoperative monitoring of facial and cochlear nerve function,[16] tumor removal with preservation of facial nerve function is feasible in most cases and preservation of hearing is feasible in selected cases. When it is not possible to remove a tumor from the cochlear nerve, subtotal removal and decompression of the internal auditory canal may delay hearing loss.

When bilateral loss of auditory function has occurred, vibrotactile devices may prove to be helpful sensory aids. The addition of a device that provides information regarding prosodic features of speech can enhance a patient's receptive communication abilities. The introduction of multichannel tactile aids promises to provide added benefit by providing a spatial array that may permit a tactile aid to provide spectral information. Experimental protocols such as cochlear nucleus implants are under evaluation and may prove helpful in the future.[17] When attempted hearing preservation operations have been unsuccessful but the cochlear nerve remains, cochlear implantation may prove to be yet another alternative (N. Cohen, unpublished observations, 1990).

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MEASUREMENT OF HUMAN COCHLEAR BLOOD FLOW

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Cochlear blood flow (CBF) was measured with a laser-Doppler (L-D) flowmeter (Periflux PR2-B) in four unanesthetized human subjects with chronic tympanic membrane perforations and nine anesthetized human subjects undergoing middle ear operations. The L-D recordings were made over the promontory and/or the round window membrane during carbogen breathing and direct electrical stimulation of the cochlea in both groups and with warm water irrigation of the external ear canal in the anesthetized subjects. Carbogen led to little or no change in CBF as monitored with either measurement approach in either subject group. Electrical stimulation yielded an increase (15% to 25%) in CBF as recorded from the promontory in seven of the nine subjects tested. Warm (44°C to 49°C) water irrigation produced changes of 20% to 60% in CBF that were partially recoverable in the 10 minutes available for study. This study demonstrated the feasibility of direct CBF measurement in humans with the L-D method. Moreover, the data indicate that carbogen has little influence on CBF and that electrical stimulation at relatively safe levels and warm water irrigation of the ear canal produce increases in human CBF.

KEY WORDS — carbogen breathing, cochlear blood flow, electrical stimulation, human subjects, laser-Doppler flowmetry, temperature variation.

INTRODUCTION

Speculation on the role of cochlear vasculature changes in sensorineural hearing loss has a long tradition in otolaryngology. Most of our views reflect histologic studies of postmortem changes in the vasculature of pathologic human temporal bones or experimental animal material. Thus, Johnsson and Hawkins[1] and Schuknecht[2] have provided data that support a vascular basis for some forms of presbycusis, showing loss and atrophy of the cochlear vessels. Vertes and Axelsson[3] and Dengerink et al[4] measured several vascular parameters on surface preparations of cochlear vessels. Images of vasoconstriction and reduced red blood cell counts suggested an overall decrease in cochlear blood flow (CBF). Duvall et al[5] and others have also shown a potential role of vascular changes in noise-induced hearing loss. These and other studies of otopathology, as well as consideration of general homeostatic mechanisms of the body, support the notion that any inner ear disorder with a significant local metabolic component will be influenced by the state of the cochlear vasculature. To the extent that this notion is valid, the enhancement of CBF offers an effective treatment for these inner ear disorders.

Meniere's syndrome, presbycusis, noise-induced hearing loss, certain other forms of trauma-induced hearing loss, and some sudden hearing loss may all be affected by CBF. Accordingly, treatments that are presumed to affect CBF have been attempted in many cases of these disorders, with promising but variably successful outcomes.[6-11] In many cases interpretation is hampered by the variable course of some of these disorders and the relatively high spontaneous rate of recovery observed. In all cases these interventions are hampered by the relative lack of information on the effect of various treatments on CBF in humans. Technical developments during the last two decades have resulted in new measures of CBF,[12] new efforts to study CBF, and new insights into the dynamics of CBF and its control.[13] Systematic studies with microspheres, intravital microscopy, and laser-Doppler (L-D) measures in animals have demonstrated that various classes of agents such as pentoxifylline,[14,15] dilating agents,[16] osmotic diuretics[17] (also D. L. Baldwin et al, unpublished observations, 1990), electrical stimulation,[18,19] hemodilution,[20] and carbon dioxide (CO_2) breathing[21,22] may directly increase CBF. These data suggest that these agents may be of therapeutic value in humans. One reservation on this conclusion is the validity of generalizing the results from animal preparations to humans.

Of the strategies for study of CBF, the L-D measure, which provides a dynamic and proportional measure of flux, is relatively noninvasive. This technique permits study of CBF through the intact lateral wall of the cochlea. The measure has been applied in guinea pigs,[23,24] rats,[25,26] and monkeys (J. M. Miller, unpublished observations, 1990). Most recently Scheibe et al[27,28] have applied L-D techniques in humans, and provide data indicating a

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transient decrease in CBF with breath-holding. However, with a concern for the contribution of middle ear mucosa blood flow to the L-D output, these authors suggest caution in interpreting their results. Certainly the demonstration of a measure of the dynamic response characteristics of CBF in humans may permit study of important basic and clinical questions, including the validity of manipulations and agents expected to increase CBF.

The purpose of this study was twofold: to extend the initial findings of Scheibe et al and determine if the L-D method can be used to measure CBF in humans, and if so, to evaluate certain agents that may increase CBF. The investigation was performed in three phases. The first phase was to evaluate, prior to human study, any potential damage that may be done to the cochlear vasculature or threshold sensitivity of the organ of Corti with prolonged L-D measurement of the CBF in guinea pigs. The second phase was performed in four human subjects with chronic perforations of the tympanic membrane. The effects of carbogen respiration and direct electrical stimulation of the cochlea on the L-D–measured CBF were studied in these unanesthetized volunteers. In the third phase, L-D measurements were performed during a middle ear operation in anesthetized subjects. The effects of manipulation of inspired CO_2, direct electrical stimulation of the inner ear, and warm water irrigation of the external auditory meatus were studied in these subjects.

METHODS

ANIMAL INVESTIGATION

Young (200 g to 400 g) Hartley guinea pigs were used in this study. The middle ear in all animals was free of infection, as assessed directly via the operating microscope, and all had normal Preyer reflexes. The operation was performed under general anesthesia with Nembutal Sodium (15 mg/kg) and Innovar (0.4 mL/kg); supplemental anesthesia was given as a half dose every 2 and 1 hours, respectively. The basal turn of the cochlea was exposed via a posterior-ventral approach while the drum membrane and the ossicular chain were kept intact. The head was stabilized, a silver ball recording electrode was positioned on the round window membrane (RWM), and then the 0.7-mm probe of the L-D TSI (TSI Laser Flow, St Paul, Minn) was placed on the first turn of the cochlea, over approximately the 20-kHz region of the organ of Corti. A 1.27-cm Bruel & Kjaer condenser microphone driven as a speaker was coupled to the external auditory meatus via a minimum volume couple. Fifteen-millisecond tone bursts (4 kHz to 32 kHz) with 1-millisecond rise-fall time were used to elicit eighth nerve compound action potentials (CAPs). Stimulus generation and CAP recording equipment was standard and has been previously described.[29]

In these animals the thresholds for CAP responses were measured at 4, 8, 16, 24, and 32 kHz. The responses to 256 stimulations were averaged. At threshold, the magnitude of the signal ranged from 1 to 4 μV depending on the noise level for a given experiment. For any one experiment the criterion voltage for threshold was constant. The L-D probe was then placed on the cochlea for a 1-hour period during which stable CBF was measured with no cardiovascular manipulations. The CAP thresholds were again measured following this 1-hour L-D measurement period. After these physiologic observations the animals were killed painlessly with Uthol and their temporal bones were removed, intrascalarly perfused with paraformaldehyde, and post-fixed. The bone over the lateral wall membranous structures subjacent to the L-D measurement site was removed and soft tissue structures of the lateral wall were exposed and mounted on slides for light microscopic study.

CHRONIC (UNANESTHETIZED) HUMAN INVESTIGATIONS

Four subjects, three men and one woman with ages ranging from 63 to 76, routinely seen as patients in the Audiology Clinic of the Sodersjukhuset in Stockholm, volunteered for this study. The subjects all demonstrated chronic tympanic membrane perforations that occupied a significant portion of the membrane, usually more than 50%. Their bone conduction thresholds were appropriate for their age. In all cases the middle ear was free of infection and dry. Via these perforations, easy access was available to the promontory or the area of the round window (RW) by means of a straight 0.7-mm L-D probe of the Periflux 2-B flowmeter (Perimed, Stockholm, Sweden). In these studies the middle ear mucosa overlying the cochlea was intact and appeared normal.

Measurements were performed with the subject comfortably positioned on his or her back with the head on a pillow and rotated 45° to 50° to raise the ear to be studied. The L-D probe was positioned manually and fixed in place by a holder modified from a head mirror band, with additional elastic bands to stabilize the L-D probe, which extended approximately 6 cm beyond the pinna. A small amount of petroleum jelly was placed on the tip of the probe to better optically couple the device to the tissue. In addition, in each subject a platinum-iridium needle electrode was positioned in the niche of the RW and stabilized with packing or held manually while sinusoidal trains were injected into the tissue between the RW electrode and a skin electrode on the ipsilateral mastoid. The charge-balanced current was generated by an electrically isolated constant current stimulator under computer control. The stimulation system is a promontory testing device used as part of an ongoing cochlear implant program using the Vienna/3M electrode at the Sodersjukhuset under the direction of one of the

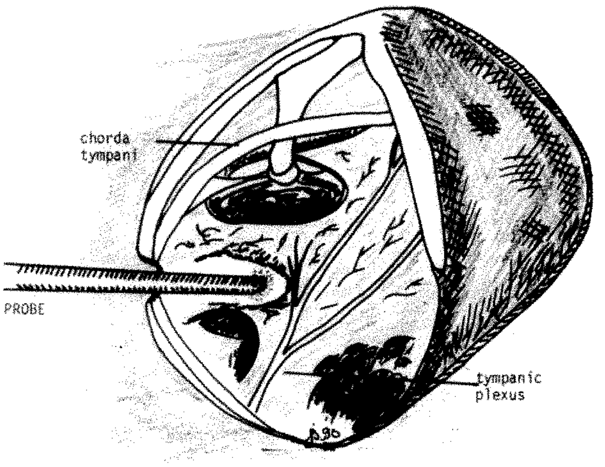

Fig 1. Illustration of surgical field for laser-Doppler studies in surgical subjects.

current authors (G.B.). The equipment has been previously described.[30] The currents employed in these studies are those used routinely in the selection and testing of cochlear electrode implant patients. In addition to the examination of electrical stimulation on L-D–recorded CBF, the effects of carbogen (10% CO_2 and 90% O_2) breathing were also investigated. In these studies, the subject was instructed to breathe at a comfortable rate while holding the carbogen mask. Thus, the subject was able to terminate carbogen breathing at any time.

Baseline L-D measures were taken following positioning of the subject and equipment and familiarization of the subject with each of the manipulations. The effects of repeated (two to five) exposures to 3 to 5 minutes of carbogen breathing on L-D output were measured and each exposure was followed by a 2- to 10-minute rest period. These carbogen studies were performed in two of the four subjects. The effects of electrical stimulation were examined in all four subjects. In each case following a period of 1 to 4 minutes of stable baseline measurement, we examined CBF changes to relatively brief (1- to 2-minute) exposures to electrical stimulation at levels from 100 to 500 μA at frequencies from 100 to 750 Hz. This frequency range of electrical stimulation selected for study was based on previous animal investigations clearly indicating that the electrically elicited CBF response was most sensitive to stimuli in the range of 500 Hz.[31]

ACUTE (ANESTHETIZED) HUMAN INVESTIGATIONS

Nine volunteer subjects undergoing operations for section of the chorda tympani and tympanic plexus for control of drooling in the Department of Otolaryngology at Turku University, Finland, were used in this study (surgeon, J.S.). There were no unusual medical conditions or medications associated with this group that might have influenced the measurements of this study. All demonstrated normal hearing and normal middle ears at the time of operation. For the purposes of this operation, the posterior ear canal skin and tympanic membrane were elevated and reflected anteriorly to expose the promontory and, in most cases, to permit visualization of the RWM. A small groove, less than 1 mm, was created along the posterior bony canal wall to permit stable positioning of the L-D probe (Fig 1). A small amount of bone wax secured the L-D probe in the groove. For all subjects, L-D measurements were made with the probe positioned on the promontory, approximately 2 mm anterior and inferior to the anterior lip of the oval window. This position centered the tip of the probe over the lateral-wall capillary beds and spiral prominence. Since, for the purposes of the operation, exposure of the tympanic plexus required removal of some middle ear mucosa and at times some drilling, the L-D probe was positioned directly on the bone and, in all but the first subject, in a slight depression in the bone. On two occasions, measurements were also made with the probe positioned in the RW niche. Positioning of the probe for these measurements was made possible by use of a 0.7-mm L-D probe with a 45° curve 3 mm from the tip. In all measurements a small amount of sterile petroleum jelly was applied to the probe tip to enhance optical coupling.

A platinum-iridium needle electrode or coiled silver electrode was positioned in the RW niche for electrical stimulation through the external auditory meatus. Stimuli were similar to those described above, but were generated by a battery-powered isolated and charge-balanced constant current device developed in-house. (This device was designed by Chris Ellinger of the Kresge Hearing Research Institute, University of Michigan. Specifications and circuit description are available.)

In these subjects, in addition to the study of electrical stimulation and the effects of variation in CO_2 breathing, the effects of warm water irrigation of the external auditory meatus were examined. For this purpose a Brookler-Grams model DA-200 closed loop caloric water irrigator was used. With the L-D probe in place, the eardrum and the skin of the ear canal were replaced in their normal position and the sterilized silicone rubber tip of the Brookler-Grams irrigator was manually placed and fixed in the ear canal. The canal was irrigated with water at temperatures of 31°C to 37°C or 44°C to 49°C for periods of 1 to 4 minutes.

Because of the time limitations imposed by the surgical considerations, not all of the manipulations were made in all subjects. Typically, we attempted to include at least two of the three studies in each subject and to examine at least one repetition of each manipulation in each subject. Overall, the effects of carbogen breathing were examined 12 times in five patients; electrical stimulation was examined 28 times in six patients; and warm water irrigation

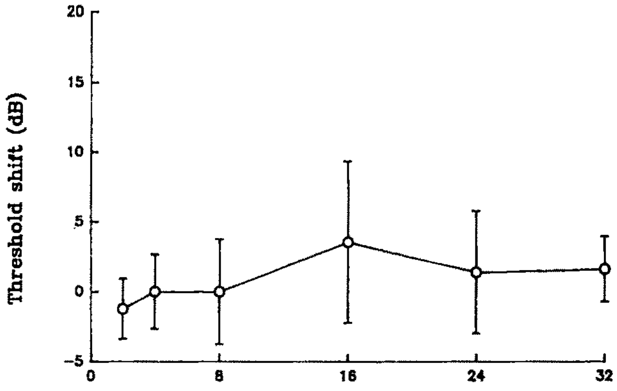

Fig 2. Change in auditory thresholds following 1 hour of continuous laser-Doppler measurement of cochlear blood flow. Function represents mean ± SD of seven subjects.

of the ear canal was examined 27 times in eight patients.

HUMAN SUBJECT CONSIDERATIONS

All protocols involving the human subjects used in this investigation were reviewed and approved by the ethics committees of the Sodersjukhuset, Stockholm, and University Central Hospital, Turku. In all cases, the L-D probe was positioned at one site for less than 1 hour, although in the unanesthetized human studies the investigation in two instances continued for 1.5 to 2.5 hours. The unanesthetized human subjects (Stockholm) all had a conductive hearing loss (due to perforation of the tympanic membrane) with a moderate sensorineural hearing loss appropriate to their age. The anesthetized subjects (Turku) all exhibited normal hearing or a mild sensorineural hearing loss. In all cases hearing was tested before and after participation in this study, particularly at higher frequencies. Repeat audiometric sensitivity was found to be within the error of measure of the test. In the study of electrical stimulation in unanesthetized subjects, all were exposed to intensities that were above their electrophonic hearing threshold. In no case did the sensation cause pain or discomfort, although in one subject the hearing sensation produced some anxiety.

RESULTS

ANIMAL INVESTIGATIONS

Figure 2 illustrates the change in mean threshold sensitivity for tone burst–generated CAP responses measured before and immediately following 1 hour of continuous measurement of CBF in the guinea pig cochlea (n = 7). The 4-dB change in sensitivity observed at 16 kHz is within the error of measurement of the system at higher frequencies for repeat observations. Careful examination of the stria at the site immediately subjacent to the L-D probe revealed no indication of vascular disorder.

UNANESTHETIZED HUMAN INVESTIGATIONS

Carbogen Breathing. Repeated observations of the effects of carbogen breathing for periods up to 5 minutes in the first two subjects studied revealed no detectable change in L-D–measured CBF. By comparison, clear changes in CBF were observed with electrical stimulation, and thus our principal study effort in these subjects focused on that variable. Carbogen breathing was not tested in the last two subjects.

Electrical Stimulation. In one of the four subjects L-D output increased significantly, with a very short latency, immediately following the onset of electrical stimulation above the subject's hearing threshold. The latency of this effect was inconsistent with previous observations in animals of the electrically evoked CBF change.[18,19] This subject also was the one who reported some anxiety at hearing the electrically elicited sound, and thus we attribute this rapid L-D increase to a small movement or blood pressure change associated with a startle or stress response to the auditory sensation.

In the three other subjects a delayed gradual increase in L-D output was observed with electrical stimulation. Figure 3 demonstrates three responses measured in two subjects. The responses demonstrated a latency from onset of stimulation to plateau of the L-D output change of approximately 1 to 1.5 minutes. With stimulation, the CBF response was maintained and the magnitude of the response was dependent upon the intensity of electrical stimulation, although it was not possible to generate careful dose-response functions because of time limitations. Figure 3A shows an 18% change in CBF observed with 90-μA stimulation at 500 Hz. The threshold for hearing in this subject was 60 μA. The threshold for a CBF response was 70 to 75 μA (extrapolated). Clear responses could be observed with intensities of less than 3 dB above the threshold for hearing, which ranged from 20 to 60 μA in these subjects at 500 Hz. Figure 3B illustrates the effect of gradual onset and then the maintained nature of the response. The threshold for this response in this subject was approximately equivalent to the threshold for hearing. As shown, at 13 dB above threshold a 45% increase in CBF was observed. Typical CBF responses at 6 dB above threshold were approximately 20%; and the largest response observed is that illustrated in Fig 3C, a 60% change in CBF. This response was obtained at approximately 10 dB above the estimated thresholds for both the CBF response and electrophonic hearing. It should be noted that because of time limitations, systematic repeated observations could not be made to carefully define the threshold for the electrically elicited CBF response. These values were extrapolated from the two to four intensities that were examined in each subject. Nor were the thresholds for electrophonic hearing precisely measured; however, the estimates, based on an ascending method of limits when the stimuli were first applied, were clear and

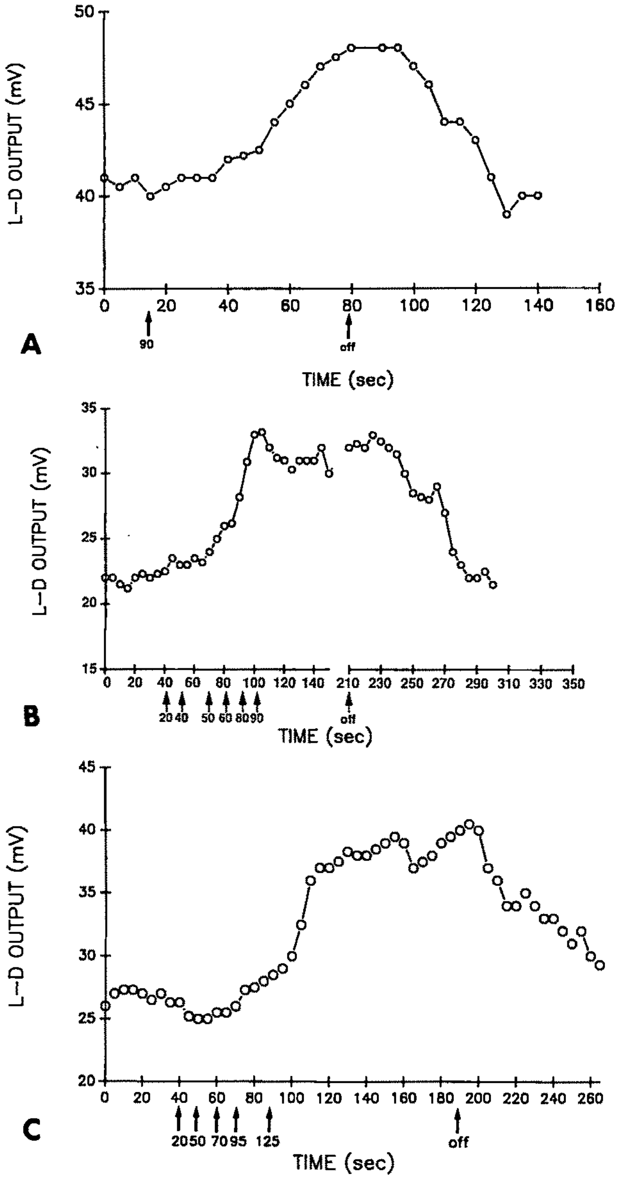

Fig 3. Laser-Doppler (L-D)–measured cochlear blood flow (CBF) during electrical stimulation via extracochlear round window electrode in unanesthetized human subjects with chronic tympanic membrane perforation. A) Representative CBF change (18% above baseline) with relatively low-level stimulation, 90 μA at 500 Hz; 4 dB hearing level, electrophonic hearing. B) CBF change with gradual onset and maintained stimulation. C) CBF change observed, 60% above baseline with stimulation at 10 dB above threshold for CBF response.

stable.

ANESTHETIZED HUMAN INVESTIGATIONS

Carbogen Breathing. Of the 12 occasions on which subjects were exposed to breathing (under respirator control) 10% CO_2 and 90% O_2, on 4 occasions small increases in L-D–measured CBF were observed. In 7 of the 12 trials, no effect was observed, and in 1 trial L-D output decreased with carbogen breathing. In each case in which an increase was observed, it reached a peak in 2 to 4 minutes, and in 2 cases, partial to complete recovery was observed within the 3- to 5-minute period of study permitted in this investigation. The changes were on the order of 5% to 10% in all cases of observed increases. In those cases in which an increase in CBF was observed with carbogen breathing, they occurred on 4 individual trials in four different subjects and only during the first exposure of the subject to carbogen. Thus, in no case was the increase in apparent CBF repeatable. Given the small magnitude and inconsistent nature of this response, it is difficult to interpret these data as indicating a significant role for carbogen breathing in increasing CBF.

Electrical Stimulation. Electrical stimulation produced changes in L-D–measured CBF in five of the six subjects in whom it was tested. In the subject in whom no response was elicited, the stimulation electrode was of high impedance, and given the compliance voltage of the stimulator, it was not possible to pass more than 100 μA with an undistorted waveform in this subject. (This was the fourth subject tested and led to the use of a larger, low-impedance silver wire electrode in the last two subjects studied. This lower-impedance electrode allowed more than adequate currents for the last subjects studied — more than 1 mA.)

Figure 4 illustrates two representative responses from two subjects to a 500- and 400-μA stimulus at 500 Hz. The raw data are shown for these examples. The responses represent 15% and 27% changes in CBF. These responses reached a maximum 1 to 2 minutes following the onset of stimulation. Time and circumstances of study do not permit us to relate these responses to either the threshold for a CBF response or to electrophonic hearing. Continuous readings of blood pressure and pulse rate were available in these anesthetized subjects. The electrically elicited changes in L-D output were not associated with any consistent change in these systemic vascular parameters. The form and magnitude of the CBF response observed with the L-D probe directly in contact with bone, with the mucosa removed, appeared similar to those responses observed in the chronic awake subjects.

Warm Water Irrigation. Warm water irrigation of the external auditory meatus produced a variable increase in L-D–recorded CBF. The reasons for this variability were technical in nature. The L-D output is sensitive to the laser probe–tissue interface. Any mechanical changes at the site of bone contact or angle of the probe relative to the tissue will modify the L-D measurement volume and, hence, the output of the device. With initial measures of the effects of irrigation, an immediate DC shift in the baseline was observed with onset and throughout the duration of stimulation. That this was a mechanical artifact due to balloon inflation is well illustrated in Fig 5, which shows the L-D–recorded output with irrigation of the ear canal with water at 31°C. With practice, it was possible to position the

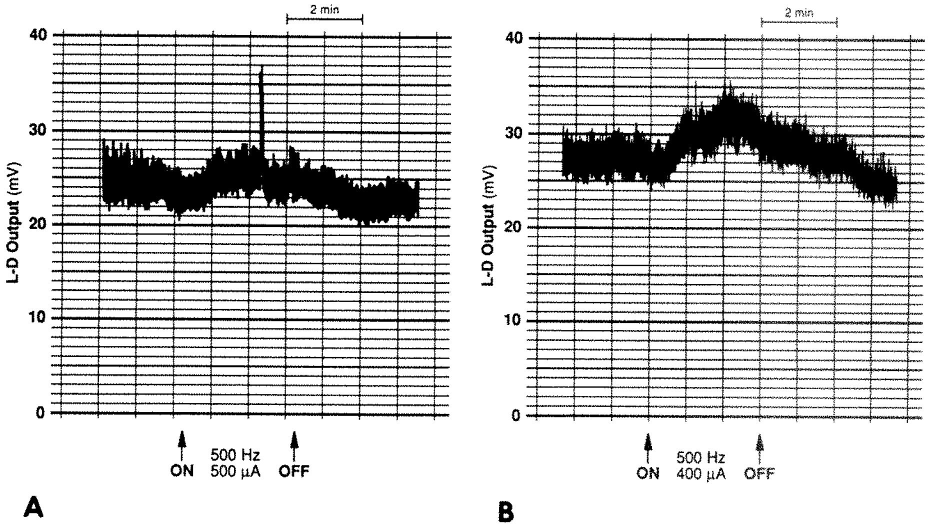

Fig 4. Cochlear blood flow change measured through promontory in unanesthetized human subjects during electrical stimulation of round window. A) Stimulation at 500 μA, 500 Hz. B) Stimulation at 400 μA, 500 Hz.

probe adequately to avoid such mechanical movements. Thus, Fig 6A illustrates a response observed with 2 minutes of warm water irrigation at 48°C. In this case the L-D output changed by 22% and complete recovery could be observed within a 3-minute period following offset of the irrigation. Figure 6B illustrates the change observed with irrigation of the ear canal at 49.5°C for 4 minutes. In this subject an L-D output change of more than 65% was observed. This was the largest change in CBF observed with warm water irrigation of the canal. During the 2-minute postirrigation observation interval, only partial recovery of CBF was observed. Complete recovery could not be followed owing to an accumulation of fluid in the middle ear, which produced the increased noise illustrated and compromised continued measurement of CBF.

Because of the requirements of surgery and the accumulation of fluid in the middle ear space that followed reflection of the ear canal into its normal position, it was not typical that repeated measurements of this variable could be made. One instance in which this was possible is illustrated in Fig 7. This Figure illustrates the effect on L-D–recorded CBF of four successive irrigations of the ear canal. The first three were 3 minutes in duration; the last was 4 minutes. The first, second, and fourth irrigations were at 49°C; the third was at 34°C. Each of the warm water irrigations was associated with a gradual increase in L-D output of more than 50%. The first response was approximately 80% over baseline. Following a 4-minute recovery period on the second trial, the L-D output demonstrated a 50% change; and following a subsequent cool water irrigation, the last 49°C irrigation resulted in an 80% increase in L-D output. Each warm water irrigation–elicited response recovered to baseline within 1 to 2.5 minutes.

DISCUSSION

The aim of this paper was to determine if CBF could be measured in the intact human cochlea with L-D flowmetry and, if so, if there are methods for increasing CBF in the human. Prior to application in the human, we determined if the emitted laser light of the flowmeter might harm the delicate vasculature or sensorineural epithelium. Thus, in seven guinea pigs, 1-hour L-D measurements were performed and revealed no effect on threshold sensitivity as measured by whole nerve action potentials and no change that could be observed in the lateral wall vasculature that was immediately under the L-D probe. These observations support previous findings in our laboratory during the past 8 years of investigations in which no evidence for cochlear damage or preparation deterioration was observed that could be attributed to the L-D measurement. Moreover, given the expected difference in laser light transmission through the delicate guinea pig promontory bone compared to that of the human, we can expect a reduced likelihood of damage in the human. (Scheibe et al[28] have recently reported that transmitted laser light through the human cochlear bone is approximately 25% of that

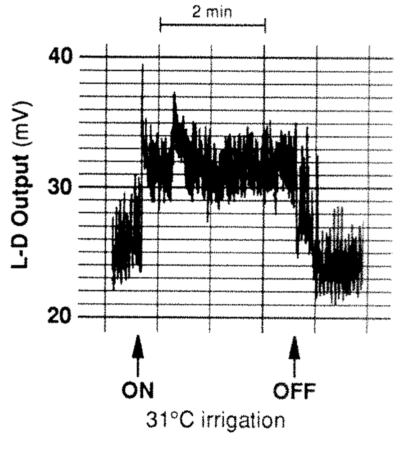

Fig 5. Laser-Doppler (L-D) output during irrigation of external ear canal at 31°C. Change in output represents mechanical artifact due to displacement of L-D probe with inflation of irrigation balloon.

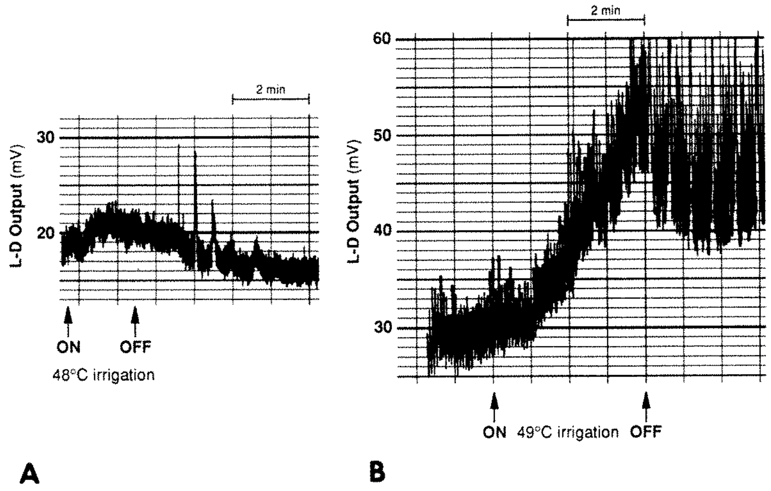

Fig 6. Change in laser-Doppler (L-D)–measured cochlear blood flow (CBF) in anesthetized human subject with warm water irrigation of external ear canal. A) Two-minute irrigation at 48°C, resulting in 22% change in CBF. B) Four-minute irrigation at 49.5°C, resulting in 65% change in CBF. Increased baseline noise after 3 minutes of irrigation represents artifact due to accumulation of fluid in middle ear.

transmitted through the promontory bone of the guinea pig.) Finally, these animal studies were corroborated by the observation that the human subjects demonstrated no change in auditory threshold following study, nor did they experience any subjective change in hearing function. We conclude that the L-D probe can be applied relatively safely to the lateral wall of the cochlea.

Three experimental variables were selected to determine if CBF could be measured in the human with L-D flowmetry. These included carbogen breathing, electrical stimulation of the cochlea, and warm water irrigation. These manipulations were selected for their relative safety, applicability within the limits of our experimental situation, the existence of theoretic or empiric data to support their effectiveness in modifying CBF, and potential clinical application.

Carbogen has long been known as a powerful brain vasodilator, and with the knowledge that the cochlear vasculature is derived from the brain, it is a reasonable assumption that this agent may increase CBF in humans. Some animal studies using the microsphere technique[21] support these speculations; other reports make this less clear. LaRouere et al[15] have shown that the small and variable effects of CO_2 on CBF in the guinea pig may be due to the ability of the subject to control P_{CO_2} levels by modifying respiration rate. Recently Kallinen et al[22] have shown that in the guinea pig, under conditions of forced respiration, consistent albeit small changes in CBF could be reliably measured with the L-D flowmeter. In the present studies, under conditions of free breathing or conditions of forced respiration, we found little evidence for a change in CBF due to CO_2 breathing and elevated P_{CO_2}, which was observed in the anesthetized subjects. These observations can be interpreted as either indicating that CO_2 breathing and elevated P_{CO_2} did not affect CBF or that the L-D measure was not sufficiently sensitive to detect the changes induced.

Local electrical stimulation of the cochlea has been observed to increase CBF in the guinea pig,[15,18,19,31] with CBF increases of up to 50% of baseline values. The CBF change has a gradual onset, plateaus at approximately 1 minute, and is then maintained. In these current studies we observed increased L-D output that followed a similar time course as that observed in the animal studies, with changes of more than 50%. The time limitations placed on these human studies did not permit observation periods longer than a few minutes; however, for up to 3 minutes a maintained change in L-D output was observed. The form and magnitude of the effect support the suggestion that the L-D flowmeter was indeed measuring an electrically evoked change in inner ear blood flow. Moreover, in unpublished observations (N. J. Brown and J. M. Miller) we have seen a maintained effect of electrical stimulation on CBF in the guinea pig for more than 1 hour, although the effect slowly decreased to approximately 30% of its initial value over a 1-hour period. That these effects can be observed with current stimulation levels in the range of operation of cochlear prostheses and can be elicited with extracochlear RW stimulation as well as intracochlear stimulation indicates that this manipulation may be of clinical utility. Finally, we note that the electrically elicited changes observed in our chronic subjects, with mucosa intact, were similar to those observed in the anesthetized subjects, in whom the mucosa had been removed. This finding indicates that the anesthesia had little effect on our CBF measurements and suggests that normal mucosa in humans does not contribute significantly to the L-D–measured CBF, although Scheibe et al[28] report that under some conditions the human mucosa can significantly contribute to L-D measurements on the inner ear.

An increase in temperature has long been known to cause vasodilation of various capillary beds. In the inner ear, Miller et al[23] demonstrated that local cooling reduces CBF in the guinea pig. Of the three variables investigated in this study in humans, warm water irrigation of the ear canal demon-

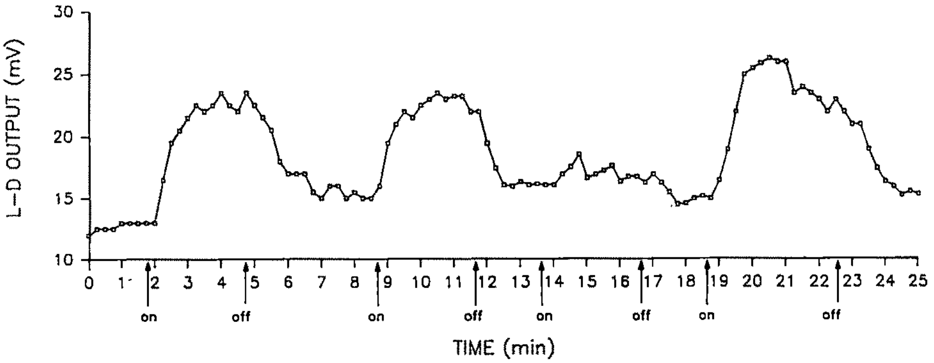

Fig 7. Change in laser-Doppler (L-D)–measured cochlear blood flow across promontory in anesthetized human subject with repeated irrigation of external ear canal. First, second, and fourth irrigations were at 49°C; third irrigation was at 34°C.

strated the most robust and consistent increase in CBF. Consistent and reliable changes of more than 50% in L-D output were observed with temperatures within the capabilities of current commercially available caloric irrigation systems. The onset of the CBF change was of relatively short latency and appeared to plateau in approximately 1 minute, although under some conditions it continued to increase somewhat during the subsequent second and third minutes of irrigation. To the extent that it was possible to continue measurements following irrigation, in all cases recovery appeared to be complete and to follow a more or less exponential time course. Control observations with irrigation at or below body temperature support the conclusion that the measured change was dependent solely on an increase in regional tissue temperature; and while it was not possible to perform parametric observations, it seemed apparent that the magnitude of the recorded CBF change was dependent on the temperature of the irrigating water. Given that these observations were made in subjects in whom the mucosa overlying the cochlear bone had been removed under the L-D probe, as was the case in some of the subjects studied with electrical stimulation, and that in some instances the L-D probe was placed in a niche in the promontory bone, it is difficult to attribute the changes observed to factors other than changes in CBF.

We note that in addition to the promontory measurement site used in all subjects, in two subjects with each of these manipulations attempts were also made to measure CBF with the L-D probe directed through the RWM. In neither case was any change in L-D output registered. These findings are similar to those that have been made in the guinea pig. The basis for this lack of sensitivity of the L-D probe to CBF as measured through the RW may be the distribution of fine capillaries versus major vessels in the measurement volume under the probe on the lateral wall versus that when the probe is placed over the RW. Because of the design of the L-D flowmeter, it is relatively insensitive to flow in large vessels. The fine capillary network of the lateral wall would appear to provide an ideal measurement volume, while the larger vessels in the modiolus may provide a less than appropriate geometry for this device.

These observations lead to the suggestion that the cochlear vasculature contributing to the L-D measurement comprises principally, if not exclusively, the vessels of the lateral wall immediately under the probe tip. Previous animal experiments demonstrate that the L-D measurement obtained with the probe positioned over the lateral wall is restricted to changes in flow in the cochlear vasculature.[12,24] In skin the measurement depth of the L-D measurement has been shown to be restricted to approximately 1 mm, with the measurement volume equal to 1 mm^3.[32] While we do not have direct data on the penetration of emitted and reflected laser light in the temporal bone, it is not likely significantly more than that on skin. LaRouere et al[15] examined the relationship of CBF as measured by the L-D flowmeter and intravital microscopy of red blood cell velocity in the lateral wall of the guinea pig cochlea. The CBF changes were induced by CO_2, electrical stimulation of the cochlea, a systemic adrenergic agent, and positive end expiratory pressure. Regardless of manipulation, they showed correlations between the L-D measurement and a multivessel analysis of red blood cell velocity of 0.8 to 0.94. Thus, almost all of the changes observed with the L-D flowmeter could be accounted for by changes in lateral wall flow. Given that these studies were performed in the young guinea pig, they indicate that even with significant reduction (70% or more) of the human lateral wall bone, L-D–measured CBF probably reflects flow changes in the capillary networks of the lateral wall.

This report supports the suggestion by Scheibe et al[27,28] that CBF can be measured with L-D flowmetry in the human. It extends their studies to demonstrate reliable and consistent changes in CBF with electrical stimulation and warm water irrigation of the ear canal. This approach provides an opportunity to now determine some of the characteristics and control mechanisms of CBF in humans with development, with aging, under normal conditions, and in the pathologic ear. Given the clinical utility of carbogen breathing, we were disappointed in the lack of effect of this manipulation on CBF. On the other hand, direct electrical stimulation of the RW would appear to be both relatively safe and effective, with few potential side effects. Most intriguing are the reliable and robust changes in CBF observed with the simple procedure of irrigating the ear canal with warm water. It would surely seem that this approach would have the fewest negative side effects and provide the least invasive and least expensive method for local increase in cochlear perfusion. The use of bilateral warm water caloric irrigation in the human may make it possible to eliminate or at least minimize vestibular effects.

Finally, we would note that for further investigations, L-D measurements in humans, as in animals, must be performed and interpreted with care. The measurement system is susceptible to artifacts. Primary among these artifacts are movement-induced changes in the position of the probe, as we observed with irrigation and as has been recorded by Thorne et al[33] with noise exposure in animals. In addition, the accumulation of fluid in the closed middle ear about the L-D probe may affect the output of the system. With care these artifacts can be minimized or avoided. In addition, while we view this demonstration that the L-D measure may be applied to the human cochlea as a significant step in our ability to study and understand normal and pathologic inner ear blood flow, it is important to remember that it provides only a relative measurement of flow in the tissues of the measurement volume. It can provide a dynamic and quantitative-proportional measure of change in CBF, but it cannot yet be calibrated in physical units, and it cannot be applied across subjects to compare the characteristics of baseline CBF in one patient versus another. Work is ongoing to develop the standards that will allow calibration of the L-D output in known physical units of flow, but the cochlear vasculature is complex and it is unlikely that the required standards will be available soon. With care in application and interpretation, we suggest that this strategy of measurement offers a means for systematic evaluation of clinical interventions that may prove useful in the treatment of metabolic disorders of the inner ear. Moreover, given the demonstrated sensitivity of L-D measurements to mechanical manipulations of vessels supplying the cochlea,[24,28] an obvious additional application may be the development of this approach for intraoperative monitoring during certain skull base operations.

ACKNOWLEDGMENTS — The laser-Doppler flowmetry equipment used in all human investigations was made available by the generosity of the Periflux Corporation, Stockholm, Sweden.

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MAGNETIC RESONANCE IMAGING AND COMPUTED TOMOGRAPHY IN PEDIATRIC HEAD AND NECK MASSES

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Fifty-three magnetic resonance imaging (MRI) and 25 computed tomography (CT) studies of 53 head and neck masses in pediatric patients were reviewed retrospectively. All lesions had pathologic proof except for 2 metastatic and 2 recurrent lesions, which only had prior pathologic confirmation at their primary sites. These included 12 malignant tumors, 23 benign tumors, 6 inflammatory masses, and 12 congenital lesions. The MRI performance ranged predominantly from good to excellent in detection of the lesion and the extent of involvement and in contrast to the surrounding tissue; when CT comparison was available, MRI proved to be equal to or better than it in detection of these factors and in preoperative diagnosis. Our results suggest that MRI should be the method of choice for the initial evaluation of the pediatric head and neck region, especially in those patients requiring multiple examinations. However, CT and MRI should be used conjunctively in complicated cases, especially those possibly involving lesions with calcifications or bony involvement.

KEY WORDS — computed tomography, magnetic resonance imaging, pediatric head and neck masses.

INTRODUCTION

Several recent studies have suggested that magnetic resonance imaging (MRI) has great potential in demonstrating normal anatomy and pathologic processes in the adult head and neck region.[1-11] Because MRI lacks radiation and generally provides excellent lesion-to-soft-tissue contrast without using intravenous contrast material, its application in pathologic processes involving the pediatric head and neck region has become more appealing, especially in young patients requiring multiple serial examinations.[12] We reviewed retrospectively MRI and computed tomography (CT) studies of 53 masses involving various pathologic processes in the head and neck region of pediatric patients to evaluate the efficacy of MRI and to compare MRI and CT in various categories.

MATERIALS AND METHODS

A total of 53 MRI and 25 CT studies in 53 patients (ranging from 1 day to 18 years of age) presenting with neck masses were reviewed retrospectively. All MRI studies were reviewed independently by radiologists (W.T.C.Y., Y.S., S.C.S.K., W. L. Smith) without knowledge of pathology results. Each lesion was evaluated in various categories, including lesion detectability, origin, margin, and extent of involvement. A score (1 = poor, 2 = fair, 3 = good, and 4 = excellent) was given in all categories by each radiologist after reviewing each examination independently. The origin of a lesion was defined as the anatomic compartment from which the lesion was most likely derived. The scores for lesion origin were based on the MRI findings: unable to define origin (0) or a probable (1), possible (2), or definite (3) origin. A final score was obtained for all categories of every lesion by averaging the scores given by all the radiologists (rounded to the nearest integer). Three top choices of differential diagnosis also were given by all radiologists with consensus in conference after the clinical history of each case was

TABLE 1. CATEGORIES OF TUMORS

Malignant Tumors (12)	*Benign Tumors (23)*	*Inflammatory or Infectious Lesions (6)*	*Congenital Lesions (12)*
Chloroma 1	Acoustic neuroma 2	Fibromatosis colli 1	Cystic hygroma 6
Chordoma 1	Dermoid 3	Giant cell granuloma of mandible 1	Dacryocystocele 2
Fibrosarcoma 1	Fibrous dysplasia 1	Inverting papilloma 1	Meningocele 1
Lymphoma 2	Hemangioma 6	Mucocele 1	Nasal glioma 1
Mucoepidermoid cancer 1	Juvenile angiofibroma 1	Ranula 1	Thyroglossal duct cyst 2
Neuroblastoma metastasis 1	Juvenile fibromatosis 1	Tuberculosis (atypical) 1	
Renal sarcoma metastasis 1	Lipoma 2		
Rhabdomyosarcoma 3	Meningioma 1		
Thyroid cancer 1	Mesenchymoma 1		
	Neurofibroma 2		
	Paraganglioma 1		
	Pleomorphic adenoma 2		

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TABLE 2. MAGNETIC RESONANCE IMAGING PERFORMANCE (N = 53)

Category	*Poor*	*Fair*	*Good*	*Excellent*
Contrast	1	1	8	43
Extent	1	0	5	47
Origin	7	4	5	37
Detectability	0	0	6	47

provided. In 25 lesions both CT and MRI were available. Side-by-side comparisons between CT and MRI were obtained in conference. Scores in all categories were given by all radiologists in conference (−2, CT much better; −1, CT better; 0, CT equal to MRI; +1, MRI better; +2, MRI much better). Twelve masses also had MRI studies immediately after intravenous injection of the contrast agent gadopentetate dimeglumine (Gd-DTPA; dose, 0.1 mmol/kg as recommended by the manufacturer). Special parental consent forms approved by an institutional review board were signed before the injection. In the 12 lesions studied by Gd-DTPA, comparison with precontrast studies was made in lesion detectability, origin, margin, extent of involvement, and tissue specificity (aid to diagnosis) by all the radiologists in conference (−1, worse after Gd-DTPA; 0, equal after Gd-DTPA; +1, better after Gd-DTPA).

TABLE 3. MAGNETIC RESONANCE IMAGING AS AID TO FINAL DIAGNOSIS (N = 53)

Lesion	*Miss*	*First Choice*	*Second Choice*	*Third Choice*
Malignant (n = 12)	5	5	2	0
Benign (n = 23)	4	14	2	3
Inflammatory (n = 6)	2	1	2	1
Congenital (n = 12)	1	10	1	0
Total	12	30	7	4

All MRI examinations were performed with either a 0.5-T (Picker International, Highland Heights, Ohio) or a 1.5-T (GE, Milwaukee, Wis) superconductive scanner. At least one T1-weighted (spin echo, 350 to 680 milliseconds; echo time, 20 to 26 milliseconds) and one T2-weighted (1,800 to 2,500 and 80 to 100 milleseconds) sequence were

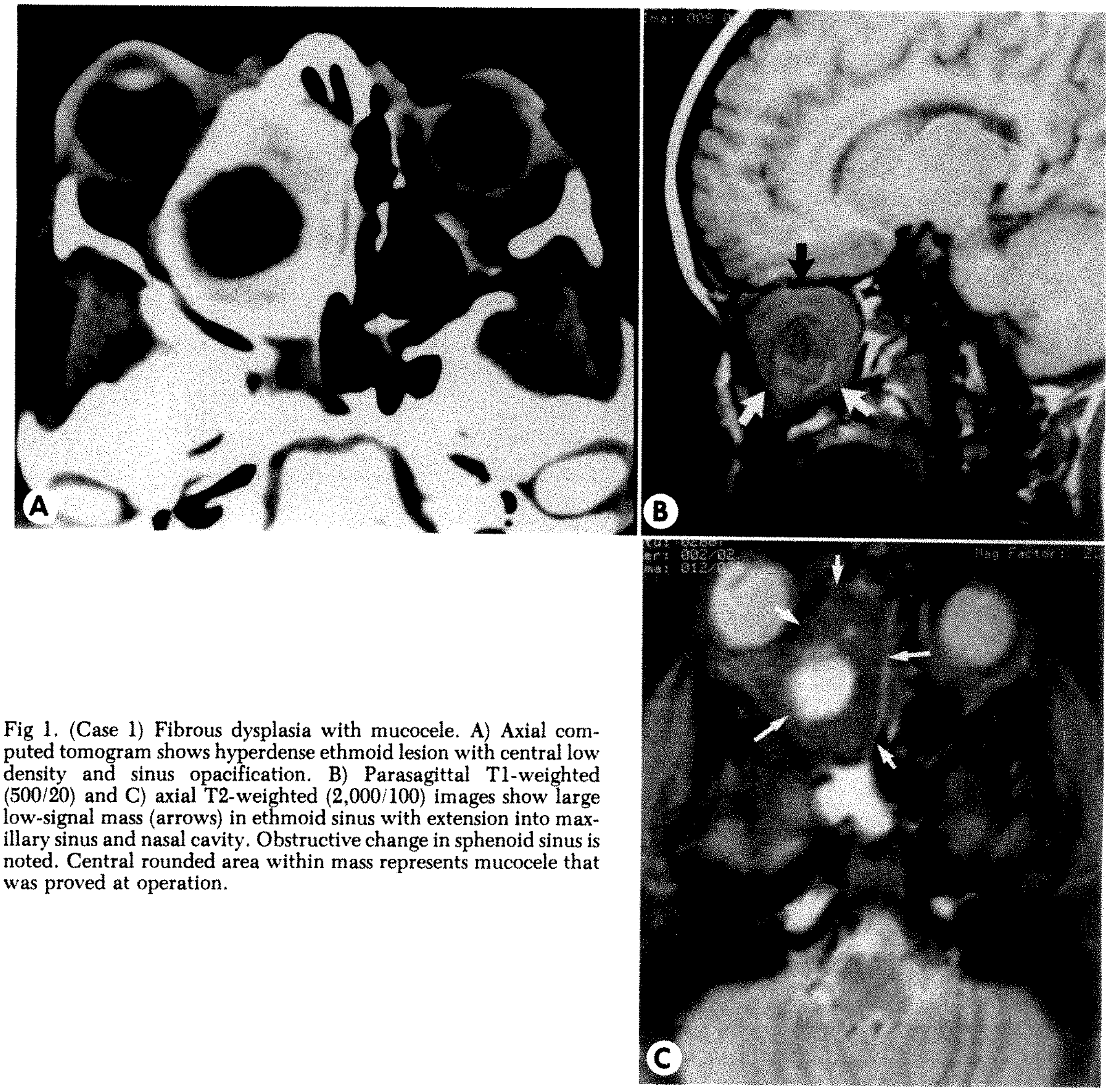


Fig 1. (Case 1) Fibrous dysplasia with mucocele. A) Axial computed tomogram shows hyperdense ethmoid lesion with central low density and sinus opacification. B) Parasagittal T1-weighted (500/20) and C) axial T2-weighted (2,000/100) images show large low-signal mass (arrows) in ethmoid sinus with extension into maxillary sinus and nasal cavity. Obstructive change in sphenoid sinus is noted. Central rounded area within mass represents mucocele that was proved at operation.

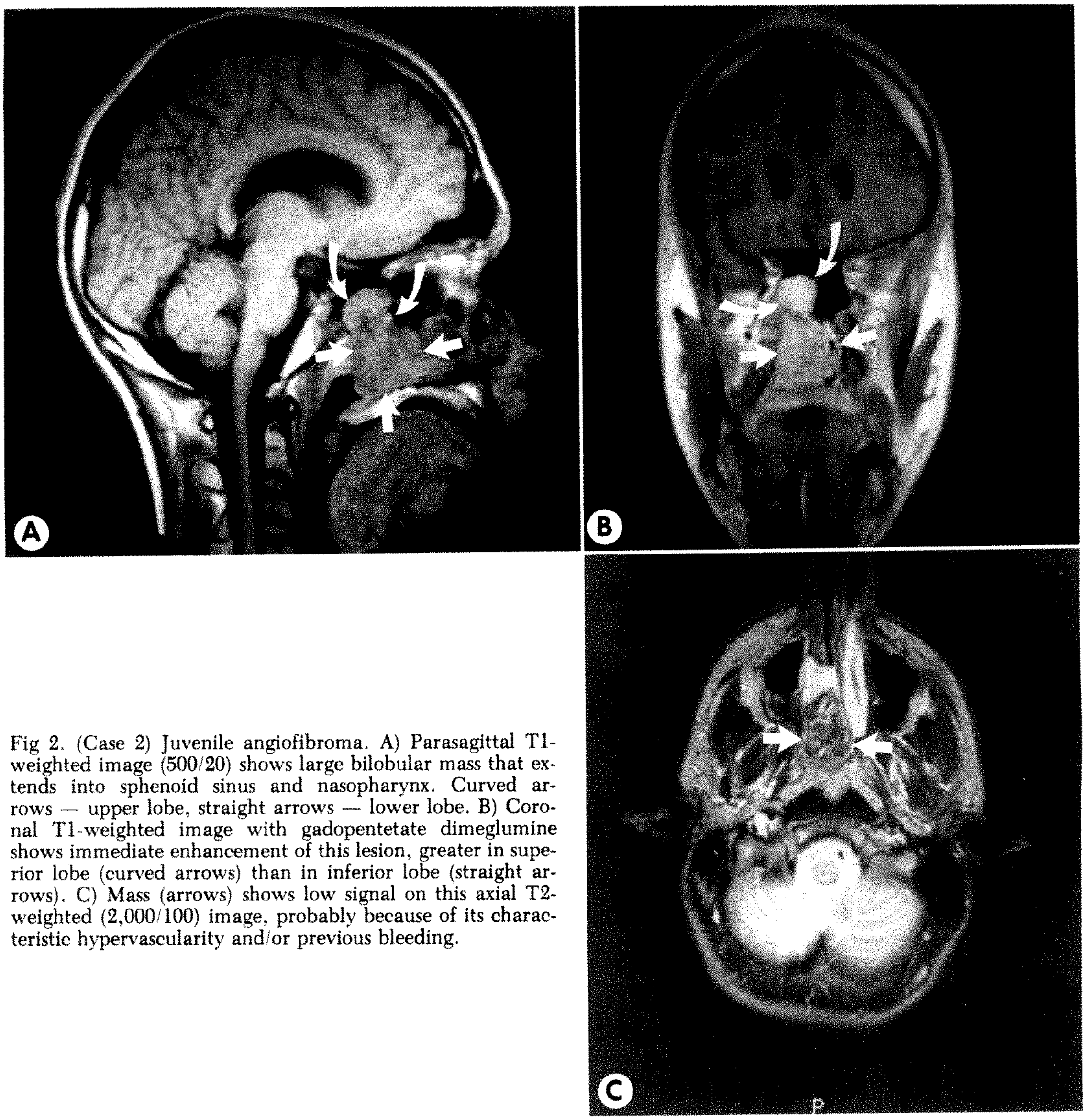


Fig 2. (Case 2) Juvenile angiofibroma. A) Parasagittal T1-weighted image (500/20) shows large bilobular mass that extends into sphenoid sinus and nasopharynx. Curved arrows — upper lobe, straight arrows — lower lobe. B) Coronal T1-weighted image with gadopentetate dimeglumine shows immediate enhancement of this lesion, greater in superior lobe (curved arrows) than in inferior lobe (straight arrows). C) Mass (arrows) shows low signal on this axial T2-weighted (2,000/100) image, probably because of its characteristic hypervascularity and/or previous bleeding.

obtained in each examination with various planes and slice thicknesses (0.5 to 1.0 cm, 10% to 50% gap in 1.5-T unit). Inversion recovery (repetition time, 1,800 to 2,500; inversion time, 400 to 600) was also performed in selected cases. All CT examinations were performed by either a Picker 1200 or a Siemens DR3 (Iselin, NJ) scanner. Imaging techniques included 4- to 8-mm contiguous axial slices.

RESULTS

All lesions were pathologically proved except for 2 distinct metastatic tumors (neuroblastoma and renal sarcoma) and 2 recurrent tumors (rhabdomyosarcoma), which only had prior pathologic confirmation at their primary sites. All 53 masses were greater than 1.2 cm in their largest diameter and were divided into four categories: malignant tumors (12), benign tumors (23), inflammatory masses (6), and congenital lesions (12) (Table 1). There were 9 types of malignant tumors and 12 types of benign tumors, indicating the great variety of benign and malignant tumors that may occur in the head and neck region (Table 1). The causes of the inflammatory or infectious masses were also diverse. Half of the congenital lesions were cystic hygromas.

The MRI performance generally ranged from good to excellent in all categories (Table 2). In the detectability category, no case was poor or fair, ie, all lesions were easily seen by MRI. All but two examinations were regarded as good or excellent in estimating the extent of involvement and providing tissue contrast with respect to the surrounding background. Both cases involved recurrent tumors in patients who had undergone prior operations, radiotherapy, and/or chemotherapy. The signals of these two lesions were heterogeneous to the surrounding tissue, and the margins of the lesions were not clearly defined (Table 2). In our series, T2-weighted images generally provided better contrast

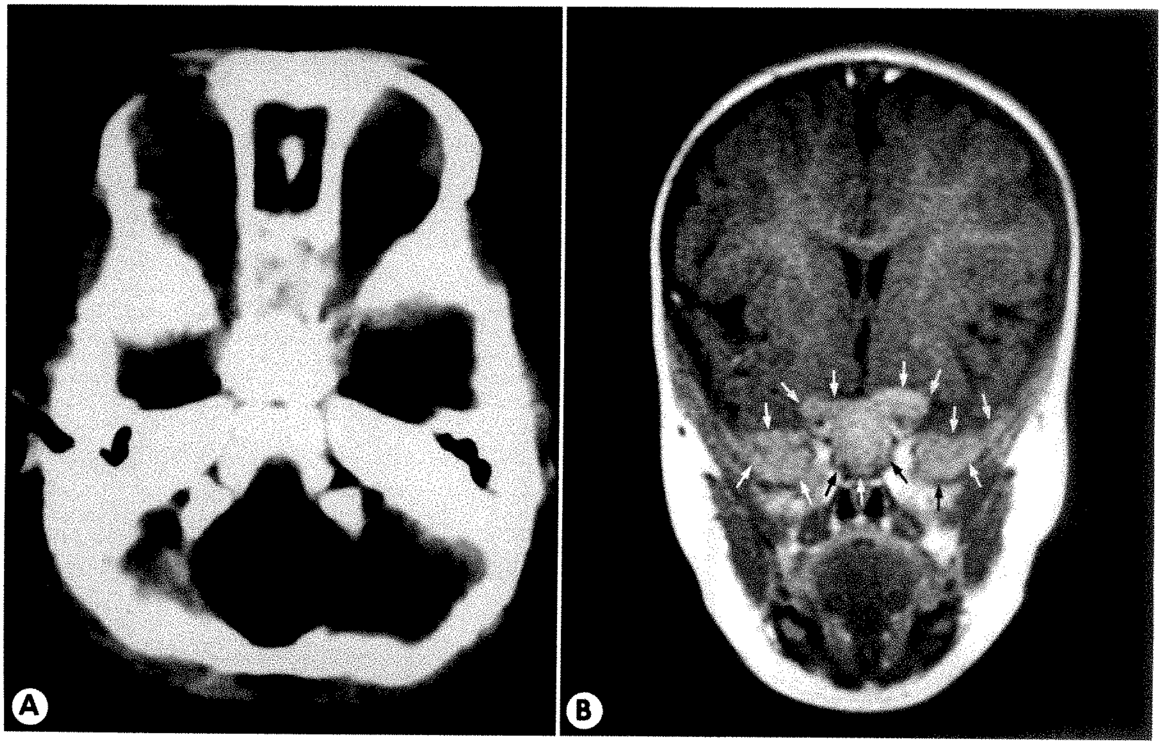


Fig 3. (Case 3) Metastatic neuroblastoma. A) Computed tomogram shows possible mass along lateral orbital wall. B) Coronal T1-weighted image (450/20) with gadopentetate dimeglumine shows enhancing lesions (arrows) involving sphenoid sinus, parasellar region, and infratemporal fossa.

than T1-weighted images (in 46 of the 53 cases), whereas T1-weighted images provided better anatomic detail (50 of 53). Therefore, both T1- and T2-weighted images were essential for estimating extent of involvement and relationship to the surrounding normal anatomic structures.

With respect to preoperative diagnosis, MRI (interpreted by a radiologist) was correct (first choice) in 5 of 12 malignant tumors (Table 3). Correct diagnosis was mostly dependent on location or origin of the lesion (except for large lesions with extensive involvement), patient age, and clinical presentation. The MRI characteristics such as signal intensity and demarcation (well or poor) of the lesion were not helpful in the diagnosis of malignant tumors or differentiation from benign tumors (Figs 1-8). However, MRI characteristics provided useful information in the diagnosis of some benign tumors and in the differentiation from malignant tumors. These benign tumors included lipoma, acoustic neuroma, neurofibroma, juvenile fibromatosis, and hemangioma. Therefore, MRI performance was slightly better in the diagnosis (first choice) of benign tumors (61%) than in that of malignant tumors (42%). Only one of six inflammatory lesions was correctly diagnosed by MRI. Generally, a homogeneous high signal on both T1- and T2-weighted images was more consistent with an abscess than a solid tumor (Fig 9). In addition, MRI characteristics could not be used reliably to separate inflammatory processes from malignancy. Magnetic resonance imaging performed well in the evaluation of congenital lesions (83%). This was especially true for cystic hygroma, which had characteristic MRI findings differentiating it from hemangioma, including multiple cystic compartments, fluid-to-fluid levels, and extremely high signal on T2-weighted images (Fig 10). In addition, structural defects related to congenital lesions were usually better demonstrated by multiplanar imaging, especially T1-weighted images. When the top three choices were all included, the rates for correct diagnosis were increased to 58% for malignant, 83% for benign, 66% for inflammatory, and 92% for congenital lesions.

In the 25 cases studied by both methods, MRI and CT were equal in performance (Table 4) in the majority of cases (range from 48% [extent] to 96% [origin] in all the categories). In most lesions, MRI performed better than CT in lesion detectability, lesion contrast, extent of involvement, and aid to final diagnosis. Magnetic resonance imaging was not useful in the detection of calcification or bony involvement. Computed tomography was better in the diagnosis of one case (Fig 1) in lesion calcification, tissue contrast, and aid to final diagnosis. Because of the absence of bony artifact, MRI was especially useful in the detection and outlining of lesions involving the skull base (10 cases), including the cerebellopontine angle, parasellar space (Fig 3), and infratemporal fossa (Figs 5, 6, 8, and 9). Magnetic resonance imaging performed better in the aid-to-final-diagnosis category of benign and congenital lesions. As compared with CT, MRI sometimes separated secondary changes from the le-

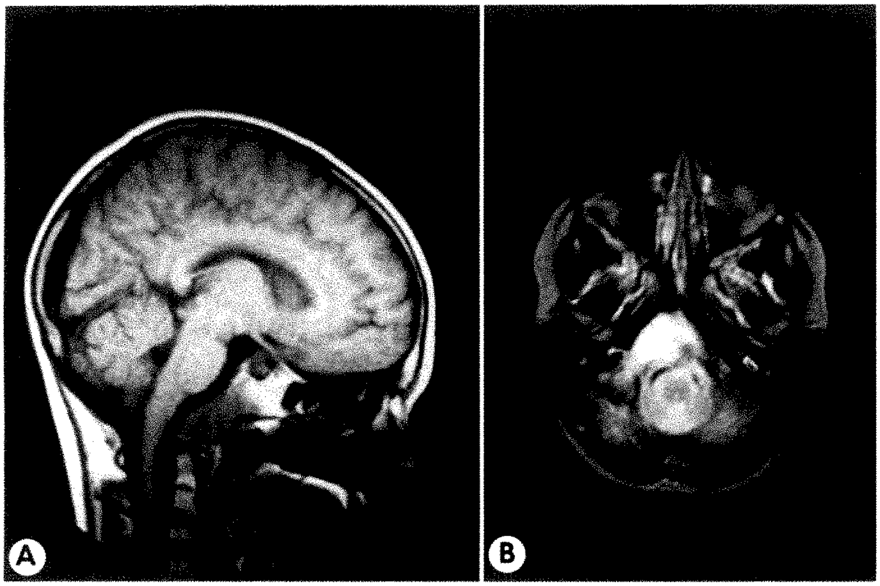
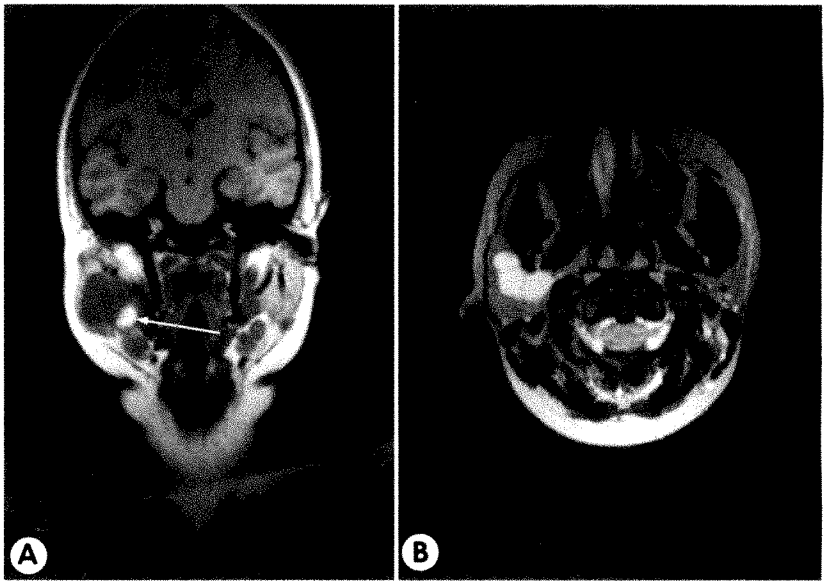


Fig 4. (Case 4) Metastatic renal sarcoma. A) Sagittal T1-weighted (450/20) and B) axial T2-weighted (2,000/100) images show metastatic lesion involving clivus and tip of odontoid process.

Fig 5. (Case 5) Pleomorphic adenoma of parotid gland. A) Coronal T1-weighted (500/20) and B) axial T2-weighted (2,000/100) images show well-defined right parotid mass with septation (B) and hemorrhage (arrow on A).



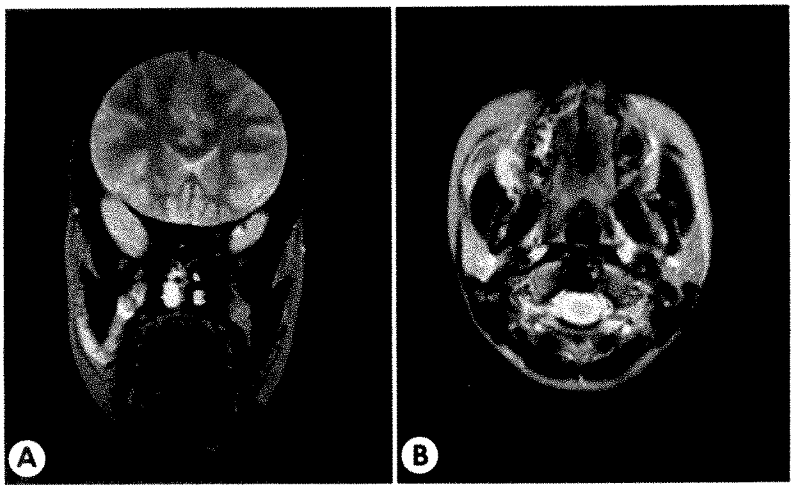


Fig 6. (Case 6) Mucoepidermoid carcinoma of minor salivary gland of buccal mucosa. A) Coronal and B) axial T2-weighted (2,000/100) images show buccal space lesion arising from buccal mucosa in oral cavity and extending to fascia between masseter and buccalis.

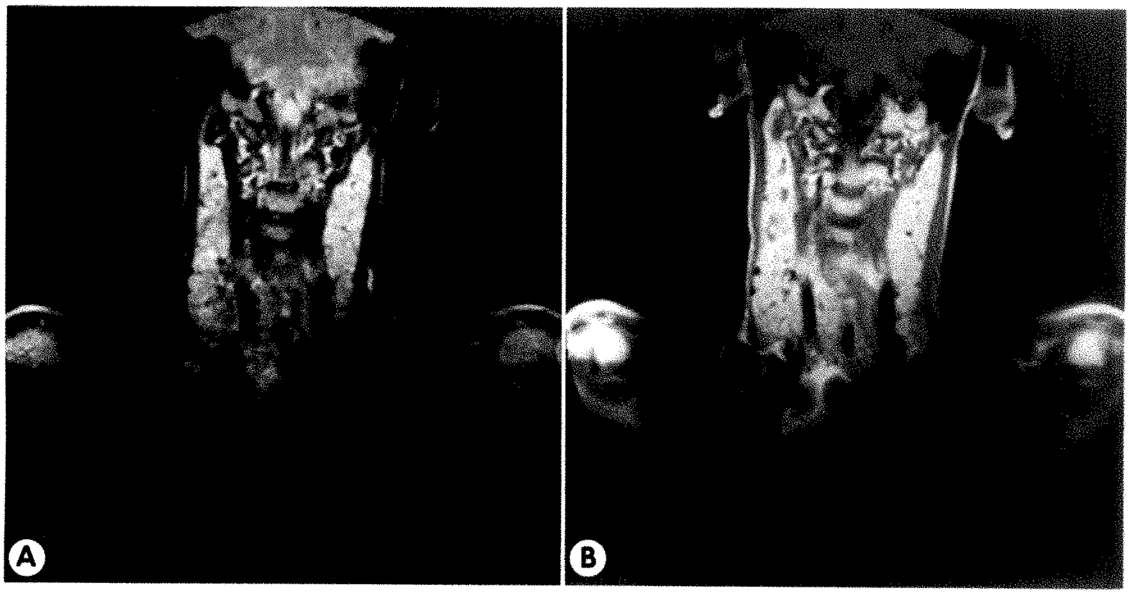


Fig 7. (Case 7) Metastatic papillary thyroid carcinoma. A) Coronal T2-weighted image (2,000/100) shows metastatic papillary thyroid carcinoma spreading to jugular lymph nodes (anterior compartment). B) Coronal T1-weighted image (450/20) with gadopentetate dimeglumine shows enhancement of metastatic lesions. Nonenhanced areas may represent relatively uninvolved lymph nodes. Thyroid gland was normal on physical examination, ultrasound, thyroid scintigraphy, and magnetic resonance imaging.

sions involving the nasal and paranasal sinuses (Fig 1). However, the bony landmarks and destruction could not be appreciated as easily with MRI. The MRI characteristics could not always differentiate between malignant lesions and inflammatory masses in the sinuses (Figs 1 and 2). Magnetic resonance imaging was useful in the evaluation of those lesions with possible central nervous system involvement or extension, especially on the T2-weighted parasagittal images, in spite of poor visualization of the fibrous tissue and bony defect. These lesions included nasal glioma, meningocele, and nasal dermoid. Use of Gd-DTPA provided additional information about tissue specificity (11 of 12 cases), especially in the differentiation of the proteinaceous necrotic center or cystic portion from a solid tumor, and a cyst or abscess from inflammatory tissue. However, Gd-DTPA MRI did not always provide better tissue contrast than the noncontrast MRI (1 better, 9 equal, 2 worse).

DISCUSSION

Computed tomography has been the established method for cross-sectional imaging in the head and neck region.[13-24] Recently, the application of MRI in this region of adult patients, including the normal anatomy and pathologic processes, has been promising. These reports suggest that the spin echo pulse sequence of MRI is at least equivalent and perhaps superior to CT in detecting and outlining extent of involvement.[1,2,7-12] In our series, MRI performance ranged predominantly from good to excellent in all categories (Table 2). As in previous studies of adult[1,3,7-11] and pediatric[12] patients, our results with pediatric patients showed that MRI provides better contrast between lesion and normal tissue and better delineation of extent of involvement than CT. However, both CT and MRI had equal difficulty in predicting the origin of the extensive lesion, which may be essential for preoperative diagnosis and planning (Tables 2 and 4). When the lesion was large, with extensive involvement of multiple anatomic divisions, MRI was not more effective in predicting the origin, in spite of better tissue contrast and multiplanar ability. As did Lufkin et al,[7] we found lesion delineation difficult in adult patients with prior surgical treatment and radiotherapy.

The MRI performance was relatively poor in preoperative tissue diagnosis (Table 3). Because measurement of T1 and T2 relaxation times and relative spin density has been reported to be nonspecific, overlap was shown between benign and malignant adenopathy.[25] Similarly, the signal intensity in our series was not a reliable indicator of malignant, benign, or inflammatory lesions. Furthermore, a well-demarcated lesion in our series may not be indicative of a benign process. Hence, biopsy is usually necessary. Because of its ability to provide excellent anatomic detail in multiple planes, MRI performed better in the diagnosis of congenital lesions, which tend to have a characteristic anatomic structure and location.

Bony structure (landmarks) and destruction or remodeling are more readily appreciated on CT than on MRI. On MRI, the primary lesion may occasionally be separated from secondary inflammatory changes within the paranasal sinuses because of differences in signal intensity on T1- and T2-weighted images and in degree of enhancement among the various tissue components. Because of

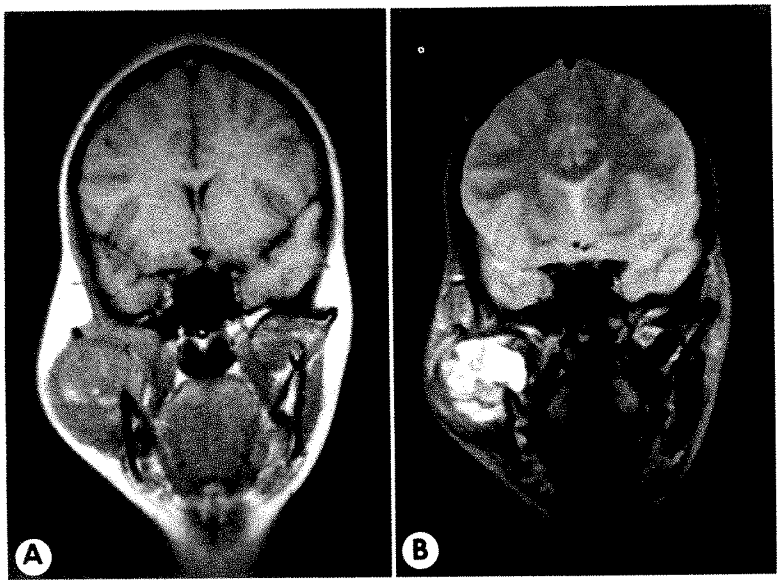


Fig 8. (Case 8) Giant cell granuloma. A) Coronal T1-weighted (TR 483/20) and B) T2-weighted (2,000/100) images show large right facial mass involving masseter, lateral pterygoid muscle, parotid gland, and mandible. Note areas of hemorrhage within lesion (A).

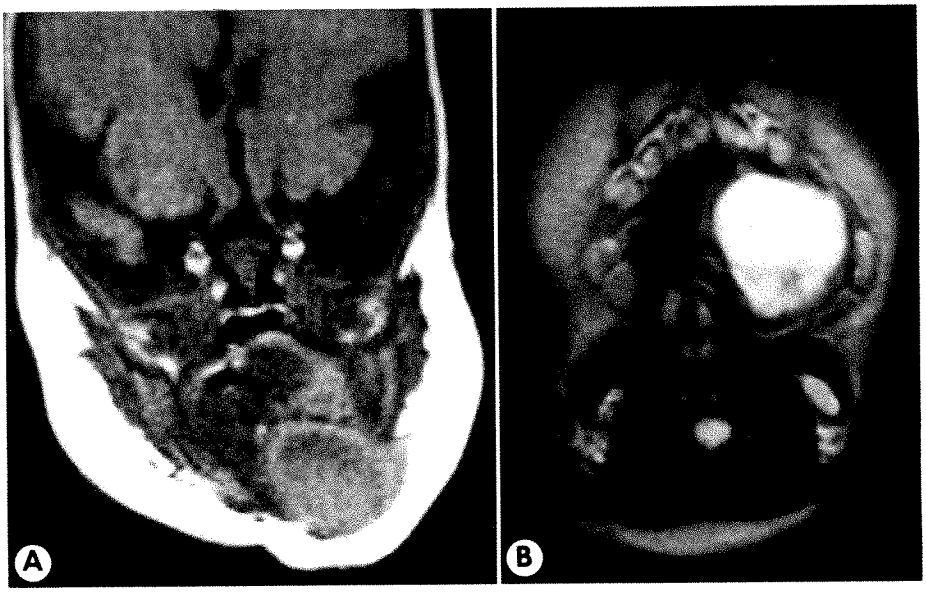


Fig 9. (Case 9) Plunging ranula. A) Coronal T1-weighted (450/20) and B) axial T2-weighted (2,000/100) images show large submandibular cystic mass with fluid-to-fluid level and relatively high signal intensity representing proteinaceous material within ranula.

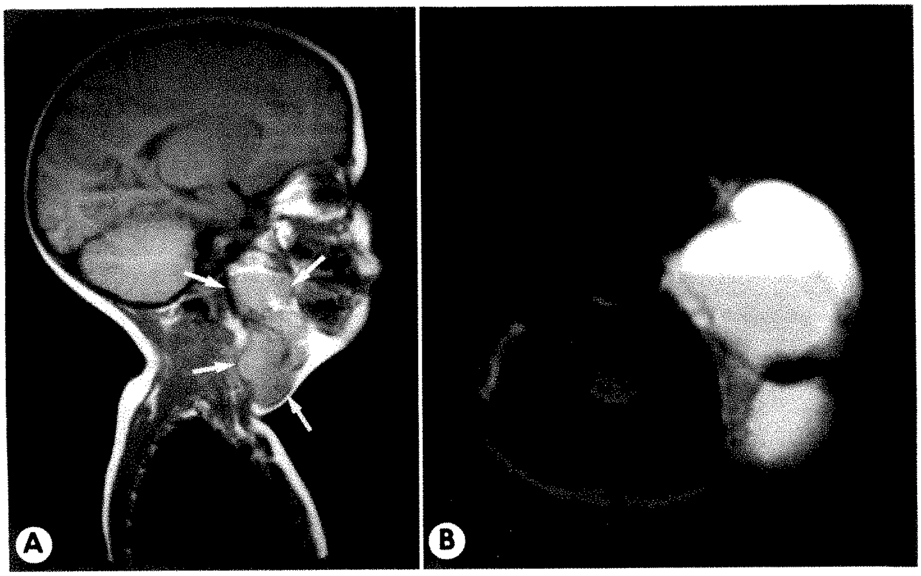


Fig 10. (Case 10) Cystic hygroma. A) Parasagittal T1-weighted image (350/20) shows large left neck mass (arrows) extending from supraclavicular region to base of skull, with signal intensity greater than that of muscle. B) Axial T2-weighted image (2,000/100) shows multiloculated cystic lesion with multiple high-signal fluid-to-fluid levels probably due to proteinaceous material, blood, and/or lipid content.

TABLE 4. RELATIVE PERFORMANCE OF MAGNETIC RESONANCE IMAGING AND COMPUTED TOMOGRAPHY (N = 25)

Category	*CT Much Better*	*CT Better*	*CT = MRI*	*MRI Better*	*MRI Much Better*
Contrast	0	1	13	11	0
Extent	0	0	12	11	2
Origin	0	0	24	1	0
Detectability	0	0	21	4	0
Aid to final diagnosis	0	1	17	5	2

the lack of bony artifact, we found that MRI was particularly useful (10 cases) in identifying lesions in the skull base, infratemporal fossa, oropharynx, and parapharyngeal region, as has been reported previously.[3-7,9]

Because of its shape, the pediatric head and neck region is more ideal to image by MRI than its adult counterpart. The adult head and neck region involves a more cylindric area. The region of interest in the adult has a relatively long cranial to caudal distance and a small cross-sectional area (compared to brain and shoulders) with significant anatomic variations. It is technically more difficult to design a surface coil with a cylindric area of interest, as in the adult head and neck region. A solenoid coil,[6,7] which lies along the z-axis (craniocaudal), cannot be applied in the superconductive unit. The pediatric head and neck region has a nearly spherical configuration, similar to the brain. We use a head coil for the pediatric head and neck area with satisfactory to excellent results. The lower field strength unit (0.5 T) is still preferred in our institution because it is less sensitive to motion artifact and interference from supporting systems such as the intravenous pump and monitor.

There is significantly more fat, bone, and air in the imaging of the head and neck area than in brain imaging. In our series, the pulse sequences involving gradient echo sequence (T2), including gradient recalled acquisition in the steady state, may not be ideal for imaging soft tissue masses because of the sensitivity to motion artifact and the susceptibility to field inhomogeneity from the interface among fat, bone, and air.[11,26]

Because a wide spectrum of diseases can occur in these rather complex anatomic structures, and MRI signal characteristics of most pathologic processes in the head and neck region are nonspecific, MRI offers limited tissue diagnosis and may not be able to differentiate among benign, malignant, or inflammatory processes. Clinical history and anatomic location are essential for the correct MRI diagnosis. Biopsy or surgical excision frequently is needed to confirm the diagnosis. However, some benign and most congenital lesions may be diagnosed and differentiated from malignant processes. With its multiplanar ability, exquisite anatomic detail, and distinctive tissue contrast, MRI provides essential information about extent of involvement for preoperative planning and posttreatment follow-up. When CT comparison was available, MRI proved to be equal to it or better in lesion detectability, lesion tissue contrast, extent of involvement, and preoperative diagnosis, and may be able to separate the lesion from the secondary changes in the sinuses. There is less technical difficulty in the sedated younger pediatric patient than in the adult because of the more spherical configuration of the pediatric head and neck region and availability of the head coil. Although our lesions were relatively large and the number of lesions was limited, our results suggest MRI should be the method of choice for the initial evaluation of the pediatric head and neck region, especially in those patients requiring multiple examinations. Both CT and MRI should be used conjunctively in complicated cases, especially those involving lesions with possible calcifications or bony involvement.

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EFFECT OF HEAD EXTENSION ON EQUILIBRIUM IN NORMAL SUBJECTS

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A dynamic posturography system was used to test the effect of 55° head extension on postural sway in 20 normal subjects. There was a highly significant increase in sway with head extension under two conditions; in both, the support surface moves proportionally to body sway angle (sway-referenced feedback). The largest increase in sway occurred when the eyes were closed and the support surface was sway-referenced. This latter condition removes vision, reduces the effectiveness of ankle proprioception, and forces the subject to depend mostly on vestibular information for equilibrium. We suggest that head extension increases sway because the utricular otoliths are put into a disadvantageous position. This may be another example of the role of utricular input in the control of balance.

KEY WORDS — head tilt, otolith stimulation, posturography, utricle.

INTRODUCTION

Imbalance and falling are common clinical complaints that may stem from disorders of several neural control systems. Despite the intuitive impression that vestibular dysfunction is frequent in such patients, it may be difficult to demonstrate by conventional examination including electronystagmography and imaging studies. Even when successful in elucidating the underlying pathophysiology, conventional evaluation tends primarily to reveal static deficits or dynamic changes that are difficult to correlate with specific clinical symptoms.

The impressive morbidity associated with falling, especially in the elderly, has recently directed attention to the possibility of dynamic postural disorders.[1-3] In these cases, dysfunction might occur only in specific situations or particular body positions. Such dysfunction could lead to falls and consequent injury in the absence of findings during conventional evaluation.

Elderly subjects, especially, may complain of dizziness, vertigo, or imbalance on looking up, a body movement common to many routine activities. Using a variety of techniques, Brandt et al[4] and Norre and Forrez[5] demonstrated increased postural sway coincident with head extension. However, the prevalence, severity, and cause of such changes remain unclear.

We considered it important to establish the range of postural sway that is induced by head extension in normal subjects before investigating other groups. This study uses a commercial device to explore the effects of head extension in normal subjects by applying a series of specific, quantitative, and reproducible maneuvers.

METHODS

Data were obtained by use of the NeuroCom Equitest dynamic posturography device, which measures postural sway in six defined test conditions using pressure-sensitive strain gauges located in each quadrant of the platform. The six defined test conditions are given in Table 1. Recent articles by Voorhees[6] and Shepard[7] provide descriptions of platform operation in more detail. The Equitest protocol attempts to evaluate the three systems that are chiefly responsible for maintaining the upright posture: vestibular, visual, and proprioceptive. The test conditions are meant to isolate the function of one system by reducing the contribution of others or by the presentation of conflicting sensory input. Thus, vision is removed in conditions 2 and 5, and proprioceptive and visual inputs are confounded by external feedback in conditions 3 through 6. The external feedback is accomplished by sway-referencing. In some test conditions, the visual surround is sway-referenced. That is, the enclosure or "visual surround" moves with any anterior-posterior sway of the test subject. When the platform or support surface is sway-referenced, the platform moves proportionally to the anterior-posterior body sway angle. However, the original testing scheme does not reduce or confound the contribution of the vestibular system. Head tilt may be useful in achieving this.

TABLE 1. SIX MEASUREMENT CONDITIONS OF NEUROCOM EQUITEST

Condition	*Definition*
1	Eyes open; fixed support surface
2	Eyes closed; fixed support surface
3	Eyes open; fixed support surface; visual surround moving with anterior-posterior sway (ie, visual surround sway-referenced)
4	Eyes open; platform support surface moving proportionally to anterior-posterior body sway angle (ie, support surface sway-referenced)
5	Eyes closed; support surface sway-referenced
6	Eyes open; both visual surround and support surface sway-referenced

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From the Rehabilitation Research and Development Center, Atlanta Veterans Administration Medical Center (both authors), and the Division of Otolaryngology (Jackson) and the Department of Neurology (Epstein), Emory University School of Medicine, Atlanta, Georgia. Supported by Core Funds from the Rehabilitation Research and Development Center, Atlanta Veterans Administration Medical Center.

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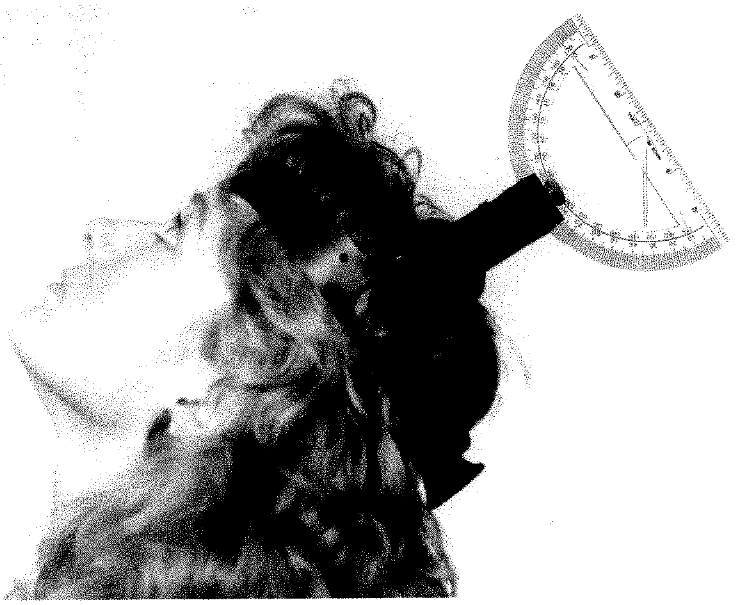

Fig 1. Inclinometer used to position head 55° from vertical.

For each condition, each subject was tested with the head normally erect and also with the head extended 55°. The inclinometer used to position the head is shown in Fig 1. Three trials were performed in each of the six conditions for both head positions. The sequence of head positions was alternated to obviate the effect of learning on performance. One subject first performed all the head-erect trials, rested for 5 to 10 minutes, and then performed the head-extended trials. The next subject would first perform the head-extended trials and follow with the head-erect trials. The three trials lasted 20 seconds each and had a short interval between them (2 to 5 seconds).

The Equitest protocol provides a calculation of center of mass sway and allows the calculation of a dynamic equilibrium score ranging from 0 to 100. No sway produces a score of 100. Sway reduces the score. A "fall" from the platform produces a score of 0. The loss of balance or alteration in stance that is considered a "fall" can manifest as a sudden step or grabbing for the enclosure to regain balance. A score of 0 can also be given when the subject sways to the maximum calculated theoretic limit. Scores for each condition were the average of three trials. Average scores were compared with head-erect and head-extended or "tilted" scores (Table 2). The paired *t* test was used for statistical analysis in all six conditions. Individual scores across conditions were compared by product-moment correlation coefficients.

Subjects were 9 women and 11 men with ages ranging from 22 to 69 years (mean, 35.6). None of the subjects had a history of neurologic disease or active otolaryngologic disease. None had symptoms of vertigo, dizziness, or dysequilibrium. They were not taking antihistamines, anticholinergic agents, sedatives, or tranquilizers. Hearing was normal and subjectively equal bilaterally. Subjects gave informed consent to a protocol approved by the Human Investigations Committee.

RESULTS

All 20 subjects had normal scores for the standard Equitest protocol with the head erect. But with the head extended, there was a highly significant difference in dynamic equilibrium scores for test conditions 4 and 5. In test condition 4, 16 of the 20 subjects showed a poorer score with the head extended. The mean difference in score was −4.05 with p< .001 (two-tailed). In test condition 5, 18 of the 20 subjects showed a poorer score with the head ex-

TABLE 2. STATISTICAL ANALYSIS OF TEST CONDITIONS AND THEIR DIFFERENCES

		Condition					
		1	*2*	*3*	*4*	*5*	*6*
Head erect	Mean	95.05	92.66	93.52	89.27	69.40	74.29
	SD	2.11	1.91	2.04	4.38	11.59	7.32
Head tilted	Mean	94.71	91.67	92.73	85.22	55.52	71.21
	SD	1.39	2.68	2.69	5.84	11.89	14.82
95th percentile		92.3	86.3	86.6	64.3	29.6	31.2
Difference, tilted minus erect	Mean	−0.33	−0.98	−0.79	−4.05*	−13.87†	−3.08
	SD	2.42	1.80	2.73	4.51	8.55	12.76

*p< .001.
†p = .0001.

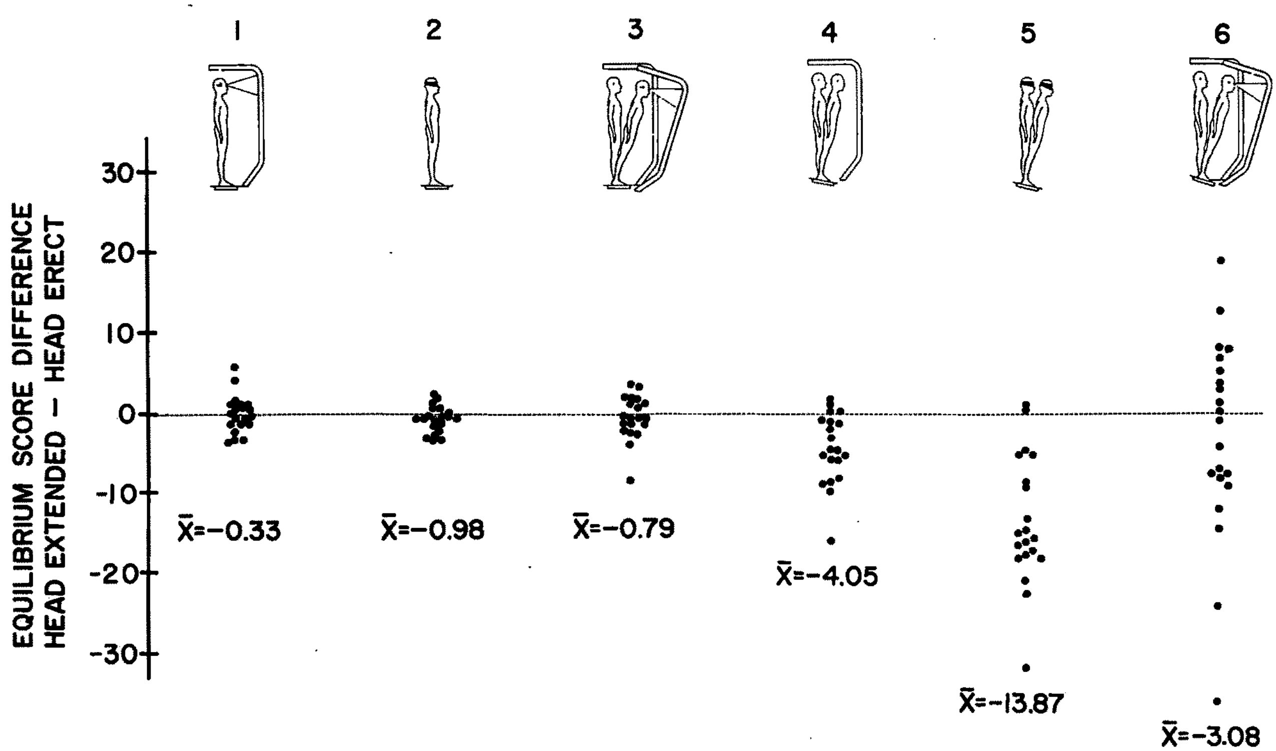

Fig 2. Test conditions 1 through 6. Each point represents equilibrium score of single subject with head extended minus that with head erect. Average values are listed below. Conditions 4 and 5 showed significant difference in mean score with head extension.

tended. The mean difference in score was −13.8 with p = .0001. Both of these differences remain significant with a nonparametric Wilcoxon rank sign test and with a conservative Bonferroni correction for multiple comparisons.[8] In accord with the usual convention for scoring posturography, we calculated 95th percentile limits of normality for head tilt; these are listed in Table 2. These values would be the lower limits for the normal population.

In reviewing the raw data, we found that fundamental frequencies of sway generally remained well below 0.5 Hz and were similar for all conditions. There was no detectable age effect. Comparison of test sequences showed no effect of learning on performance. No subjects had symptoms or signs suggesting ischemia of the brain stem or cerebellum with the head extended.

Figure 2 illustrates the differences in the dynamic equilibrium scores for head-extended minus head-erect conditions in all 20 subjects. Plots are shown for test conditions 1 through 6.

The data in condition 6 were surprising. The authors had supposed that the data from conditions 4 and 6 would be similar, even predicting that condition 6 would show a greater effect of head extension than condition 4 because we were adding the additional disruption of a sway-referenced visual signal. However, there was no significant overall trend in the dual sway-referenced condition. Instead, scatter of the data was noticeably greater. Furthermore, there was no relation between the direction of the score in condition 6 and the direction of the same subject's score in condition 3. The largest differences in scores in conditions 4, 5, and 6 were obtained from three different subjects.

DISCUSSION

Our results indicate that the majority of healthy adults, without any symptoms of neuro-otologic disease, show decreased postural stability on head extension. Although such changes have been noted before,[4,5] they had not been studied systematically in healthy individuals. Instability on head extension may have practical importance, because clinical reports indicate that injurious falls are associated with head extension in daily activity.[9]

Could our results have been affected by the inadvertent inclusion of a few asymptomatic, abnormal subjects? The changes we describe occurred in 18 of 20 subjects. The outcome could have been altered only if 1) a majority of the study population were abnormal, and 2) the changes with head tilt occurred exclusively in those subjects. This combination of events seems highly improbable.

Young et al[10] had shown previously that head orientation away from the erect position places the utricular gravireceptors in less sensitive positions, so that they are less effective in inhibiting illusions of visual tilt. Schrader et al[11] showed that head tilt in any direction inhibited postrotatory nystagmus. However, head extension had the least effect and this effect was attributed again to the disadvantageous position of the utricles.

Brandt et al[4] used a static force platform with a 10-cm slab of foam rubber placed on top of the platform and covered by a second, rigid foot support. This was meant to reduce the proprioceptive contribution of the feet and ankles and isolate the contribution of the visual and vestibular systems. The same effect is obtained more rigorously in the Equitest protocol by having the force platform sway-referenced. Norre and Forrez[5] extended these observations to patients with unilateral vestibular hypofunction and those with paroxysmal positional vertigo. They found that in some patients, eye closure and head extension provoked abnormal postural sway that was at least partially due to reduced otolithic input. Markham et al[12] also entertained this notion and pointed out that Barany and Dix and Hallpike considered benign paroxysmal positional vertigo to be due to otolith dysfunction.

We found, in agreement with Brandt et al, that head extension increases postural sway in normal subjects. However, according to the Equitest protocol, the increased sway was only evident under certain conditions. A significant difference was found only when ankle proprioception was reduced (conditions 4 and 5). It was especially prominent when, in addition, the eyes were closed (condition 5).

Brandt et al suggested two possible reasons why head extension might increase postural sway. One is intermittent basilar insufficiency caused by functional compression of the vertebral artery, particularly in elderly patients with atheromata or with cervical spondylosis[13] and osteophytes narrowing the transverse foramina.

A second possibility is reduced accuracy of data from the utricular otolith organs. Head extension might induce physiologic instability by placing the utricular otoliths beyond their working range. Head tilt has striking effects on the postrotatory vestibulo-ocular reflex, which has been ascribed to otolith input.[14] Head tilt, off-vertical axis rotation, and "barbeque rotation" all show the effects of head position on vestibulo-ocular reflexes.[15,16] Presently, other techniques are being tested to determine if they can be used for functional assessment of the utricles or to help determine the role of the utricle in the vestibulo-ocular reflex: ocular counterrolling[12] and tilt suppression of postrotatory nystagmus.[11] Both procedures depend upon placing the utricles in a disadvantageous position. Head extension has been used to isolate the utricular otolith component of the vestibulo-ocular reflex.[16] Most investigators consider the utricle more important than the saccule in the control of these reflexes. Because of the curved orientation of the saccule, fewer hair cells would be in position to respond to head extension. Thus, even though the saccule is involved, head extension effects are probably more under the control of the utricle.

Neither our subjects nor those of Brandt et al showed clinical signs of ischemia in the brain stem or cerebellum during head extension. If increased instability were due to brain stem ischemia, we would have expected imbalance to be accompanied by other neurologic symptoms, such as dysarthria, diplopia, sensory loss, or paresis. The low mean age in both series makes ischemia even less likely.

There may be other factors besides unfavorable placement of the utricular otoliths. Head extension causes measurable stretch receptor activity in the neck. This activity could disrupt postural stability. Also, because head extension is relatively infrequent in daily activity, the coordinating centers may simply lack sufficient experience to produce stability in this position.

The surprising scatter of data points in condition 6 is unexplained. One possibility is that this scatter may reflect various degrees of visual compensation. Some subjects may have greater skill at "decoding" the sway-referenced visual surround and overcoming the attempt to nullify visual input.

It would be helpful if the head extension maneuver could be used as a test of otolith function. Our mean scores for all conditions with the head erect were not significantly different from established normal values.[17] With the head erect, the mean sway score in condition 5 is 69.4%. With the head extended, the mean sway score in condition 5 is 55.5% — a difference of 13.87%. Taking the mean ± 2 SD as an approximate normal range, a difference in scores between head-erect and head-extended would suggest an abnormality if it were greater than the mean difference in our group (13.87%) + 2 SD (17.1). Thus, a difference greater than 31% in condition 5 would suggest that the subject functions relatively well in the head-erect position and might be especially susceptible to a deterioration in balance with the head extended. The 95th percentile limits could also be used for the same purpose.

In the normal subject, there appears to be a redundancy of inputs to the coordinating centers for posture. However, if any of these inputs are nullified, there may be increased vulnerability to deficits in others. Patients with sensory polyneuropathy, who lack accurate position sense in the legs, exhibit increased instability with head extension.[4] There are clinical reports of patients with dysequilibrium and falling caused by looking up toward the top shelf of a cabinet.[9] If normal younger subjects sway when sensory input is reduced, it is not surprising that some elderly subjects experience dysequilibrium. Aging is associated with gradual losses in the visual, somatosensory, and vestibular systems.[18] The loss of redundant input from the senses would seem to be most evident in the head-extended position.

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VERTICAL PARTIAL LARYNGECTOMY: A CRITICAL ANALYSIS OF LOCAL RECURRENCE

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The purpose of this study was to evaluate local recurrence following vertical partial laryngectomies in 416 patients with either T1N0M0 or T2N0M0 glottic carcinoma. Local failure was reported according to the T stage, the precise tumor location within each stage, the true vocal cord mobility, and the surgical procedure performed. No local recurrences were observed among 42 patients who underwent thyrotomy and cordectomy when the tumor was confined to the middle third of the mobile true vocal cord. Local failure occurred in 8 of 111 (7.2%) patients in whom hemilaryngectomy was performed for tumors confined to one mobile true vocal cord. There was a diverse group of lesions within each T stage that responded differently to the surgical approaches. The differences in the initial recurrence rates are discussed in terms of careful preoperative assessment and choice of surgical technique for early glottic carcinoma.

KEY WORDS — glottic carcinoma, tumor recurrence, vertical partial laryngectomy.

INTRODUCTION

Local recurrence following conservation laryngectomy for early glottic carcinoma remains a significant problem. Large series have been reported in which local failure rates have ranged from 2% to 17% for T1N0M0 and 4% to 24% for T2N0M0 lesions (Table 1[1-7]). The purpose of this study was to evaluate local failure following vertical partial laryngectomy for early glottic carcinoma. These procedures require a vertical transection of the thyroid cartilage and paraglottic space to enter the larynx, ie, thyrotomy and cordectomy or vertical hemilaryngectomy. An analysis of the patients who failed locally has been done by correlating local recurrence with the exact tumor location in an effort to elucidate trends that may allow for more accurate preoperative assessment and choice of surgical technique.

MATERIALS AND METHODS

From January 1972 through January 1984, 416 patients with previously untreated well to moderately differentiated squamous cell carcinomas of the glottis were operated upon at the University of Paris V. The age range was from 24 to 90 years. The lesions were clinically staged according to the system recommended by the Union Internationale Contre le Cancer.[8] Clinical staging relied upon the retrospective analysis of preoperative assessments that were performed over a 14-year period by more than 12 staff surgeons and 30 residents. The precise gross extent of tumor was subclassified by consensus between the surgeon and the pathologist. Clinical staging was found to be inaccurate in 4.2% of T1 and 11.6% of T2 tumors. All patients underwent either thyrotomy and cordectomy or hemilaryngectomy. Lymph node dissections were never performed; no patients received either radiotherapy or chemotherapy.

Cordectomy via thyrotomy was performed on 168 patients. The thyroid and cricoid cartilages were never resected. Tumor resection always included a subperichondral dissection of inner thyroid perichondrium from the thyroid cartilage. The decision to perform a cordectomy, an extended cordectomy (including the anterior commissure, vocal process of the arytenoid, or the floor of the ventricle), or a bilateral cordectomy was based upon intraoperative assessment of tumor extent.

Hemilaryngectomy was performed on 248 patients. A portion of the thyroid cartilage was always included with the specimen; however, the cricoid cartilage was never resected. Depending upon the tumor location and the true vocal cord mobility, a standard, frontolateral, or frontoanterior hemilaryngectomy procedure was performed.

TABLE 1. LOCAL RECURRENCE RATES FOLLOWING VERTICAL PARTIAL LARYNGECTOMIES

Authors	*Year*	*T1N0M0*	*T2N0M0*
Biller et al[1]	1971	—	5% (3/ 58)
Som[2]	1975	—	24% (25/104)
Daly and Kwok[3]	1975	10% (3/ 29)	—
Sessions et al[4]	1975	3% (1/ 36)	4% (3/ 76)
Neel et al[5]	1980	2% (4/182)	—
Liu et al[6]	1986	4% (1/ 24)	14% (2/ 14)
Kaiser et al[7]	1989	17% (46/271)	—

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TABLE 2. RATES OF LOCAL RECURRENCE

	Both Groups	*Thyrotomy Group*	*Hemilaryngectomy Group*
Tumors confined to glottis			
Middle third	0 % (0/46)	0 % (0/42)	0 % (0/ 4)
Posterior half	6.6% (1/15)	7.1% (1/14)	0 % (0/ 1)
Anterior half	9.6% (8/83)	16.1% (5/31)	5.8% (3/52)
Whole true cord	13.1% (13/99)	17.8% (8/45)	9.3% (5/54)
True cord with anterior commissure	22.7% (10/44)	16.7% (2/12)	25.0% (8/32)
Both cords without anterior commissure	0 % (0/ 8)	0 % (0/ 5)	0 % (0/ 3)
Extension beyond glottis			
Normal mobility	25.6% (23/90)	66.7% (6/ 9)	21.0% (17/81)
Impaired mobility	32.3% (10/31)	10.0% (1/10)	42.9% (9/21)

RESULTS

There were no deaths in the immediate postoperative period. Sixty-five (15.7%) local recurrences were observed. Salvage treatment controlled local recurrences in 55 of 65 (84.6%) patients. The overall local control rate was therefore 97.4% (405 of 416 patients). Three hundred ninety-two patients (94%) had a minimum of 3 years' follow-up. Eighty-seven percent of the local failures were observed by the end of the third postoperative year.

Clinical T Stage. Forty-one of the 308 (13.2%) patients with T1 lesions had local failure. Local recurrences were observed in 24 of 107 (22.3%) patients with T2 lesions.

Exact Tumor Location. When the tumor was limited to the glottis 32 of 295 (10.9%) patients had a local recurrence (Table 2). Local control was always achieved among the 46 patients with tumors confined to the middle third of the true vocal cord. When the tumors extended toward the anterior commissure or arytenoid cartilage the rate of local recurrence increased. Among the 121 patients with carcinoma that spread beyond the confines of the glottis, 33 had local failure (27.3%).

Thyrotomy and Cordectomy. Twenty-three of 168 patients (13.7%) had local failure following vertical thyrotomy and cordectomy (Table 2). Thyrotomy always controlled tumors located at the middle third of the true vocal cord. A significantly increased recurrence rate occurred as the tumors extended away from the middle third of the true vocal cord ($p<.01$). The failure rate of tumors that extended beyond the true vocal cord was significantly greater than that of tumors confined to the cord ($p<.05$).

Vertical Hemilaryngectomy. Among the 248 patients who underwent hemilaryngectomy, 42 (17%) had local failure (Table 2). When the cancer was confined to the middle, anterior, posterior, or entire true vocal cord, local failure occurred in 8 of 111 patients (7.2%). The local failure rates for tumors either reaching the anterior commissure or spreading beyond the confines of the glottis were 25.0% and 25.5%, respectively. These rates were significantly greater than those for tumors confined to the true vocal cord ($p<.01$ and $p<.05$, respectively). The failure rate for tumors with extension beyond the confines of the glottis significantly increased when impaired true vocal cord mobility was observed ($p<.05$). Although the difference was not statistically significant, vertical hemilaryngectomy controlled the carcinomas confined to the anterior, posterior, and whole true vocal cord more often than thyrotomy and cordectomy.

DISCUSSION

Local control was always achieved, in this series, when thyrotomy and cordectomy was performed on patients ($n=42$) with tumors of the middle third of the mobile true vocal cord. Tumor resection always included a subperichondrial dissection of the inner thyroid perichondrium. Higher recurrence rates following cordectomy for tumors that have extended beyond the midcord is in accordance with the experience of others.[9-11] Micheau et al[12] observed that clinical assessment of glottic cancer was inaccurate in 10% to 30% of cases. This was particularly true when the carcinoma had spread beyond the midcord region. Whole-organ sectioning has revealed that carcinomas of the glottis may be surrounded by areas of submucosal spread and carcinoma in situ.[13] These factors may contribute to the apparent need for wide surgical margins when performing cordectomy.

Impaired mobility of the true vocal cord may be caused by the weight of bulky tumors, moderate degrees of invasion of the thyroarytenoid muscle, and extension of the growth along the superior surface of the vocal cord.[14] The low rate of local recurrence among tumors in the thyrotomy group with decreased mobility may be related to the fact that impairment was due primarily to tumor bulk without deep invasion. When impaired vocal cord mobility was present the rate of local failure was significantly increased in the hemilaryngectomy group. In general these tumors had more extensive thyroarytenoid muscle and paraglottic space invasion.

The local failure rate in the present study was significantly increased when the tumor involved the anterior commissure. Squamous cell carcinoma involving the anterior commissure has the propensity to spread subglottically.[15] Kirchner and Som[16] noted eight local recurrences among 58 patients (14%) who underwent extended vertical hemilaryngectomy for glottic carcinoma involving the anterior commissure. Seven of the eight recurrences were subglottic. The absence of an easily definable conus elasticus at the anterior commissure makes this area contiguous with the subglottis.[17] The subglottis has a network of tubuloalveolar glands that open inferior to the anterior commissure and provide a route for the caudal extension of carcinoma.[18] Bridger and Nasser[19] have concluded that a wide surgical margin in the subglottis is advisable in treating glottic carcinoma with anterior commissure involvement.

The local failure rate in this series significantly increased following hemilaryngectomy for tumors extending beyond the confines of the true vocal cords. Extension was primarily to the ventricle and/or the subglottis. Subglottic invasion is often associated with contralateral extension and involvement of the cartilaginous framework.[15] Glanz[13] studied true vocal cord carcinomas with ventricular extension and noted that they tend to invade the paraglottic space with resultant vertical spread and thyroid cartilage invasion. Vertical hemilaryngectomy transects the paraglottic space and the thyroid cartilage, both of which may be involved once carcinoma has extended beyond the true vocal cords.

This study supports the premise that partial resection of glottic carcinoma requires accurate preoperative assessment. Clinical staging may be associated with a high degree of error, even following extensive workup.[20] Whole-organ sections of laryngectomy specimens have provided insight into the behavior of glottic squamous cell carcinoma.[12-16] Kirchner[21] has used this information to reduce error in clinical staging from 40% to 22%.

The T stages for early glottic cancers have a tendency to categorize a wide variety of tumors into limited groups.[22] Glottic lesions staged as T1N0M0 include cancers 1) limited to the middle third of the true vocal cord, 2) involving the whole true vocal cord, 3) extending to the vocal process or anterior commissure, or 4) reaching the contralateral true vocal cord. Similarly, tumors staged as T2N0M0 may 1) be massive or small, 2) involve the floor of the ventricle or the subglottis, or 3) present with normal or impaired cord mobility. The present study indicates that there is a diverse group of lesions within each T stage that respond differently to the surgical approaches.

Once the choice to proceed with excision has been made it is critical to select the proper surgical technique. Local control of carcinoma following a particular partial laryngectomy is highly dependent upon the precise tumor location within the larynx. We have found that glottic carcinomas with anterior commissure involvement, impaired cord mobility, or extension beyond the true cord are predisposed to local recurrence following vertical partial laryngectomy. In our opinion, an alternative technique for these carcinomas is the supracricoid laryngectomy with cricohyoidoepiglottopexy.[23] This procedure allows for complete removal of the paraglottic space and thyroid cartilage followed by physiologic speech rehabilitation without tracheostomy.[23,24] The local failure rate for T1b and T2 glottic carcinomas was 5.5% in a series of 36 patients undergoing this procedure.[23] Glottic carcinomas confined to the middle third of the mobile true vocal cord may be reliably excised via thyrotomy and cordectomy. Lesions limited to the mobile membranous true vocal cord remain amenable to vertical hemilaryngectomy.

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EFFECT OF ALDOSTERONE ANTAGONIST ON THE DC POTENTIAL IN THE ENDOLYMPHATIC SAC

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The effect of aldosterone and canrenoate, known as an aldosterone antagonist, on the DC potential in the endolymphatic sac (ESP) was examined in the guinea pig. Intravenous administration of aldosterone (1 mg/kg) induced no change in the ESP for 60 minutes after the injection. However, canrenoate, an aldosterone antagonist, produced a dose-dependent decrease in the ESP. Pretreatment with aldosterone attenuated the decrease in the ESP by canrenoate. The results suggest the possibility that aldosterone may play a role in the endolymph absorption of the endolymphatic sac.

KEY WORDS — aldosterone, aldosterone antagonist, DC potential, endolymphatic sac.

It has been reported that an anoxia-sensitive positive DC potential of 15 to 20 mV is recorded in the endolymph of the intermediate portion of the endolymphatic sac (ES) of the guinea pig.[1-3] The origin of ES DC potential (ESP) is still unknown. The previous study, however, showed a close relationship of the ESP to sodium ion transport in the ES.[3] It is well known that aldosterone stimulates sodium absorption in the kidney.[4,5] It is of interest to determine whether or not aldosterone and its antagonist have an influence on the ESP. Therefore, we examined the effect of aldosterone and its antagonist on the ESP.

MATERIALS AND METHODS

Animal Preparation and Recording Technique. Albino guinea pigs with a positive Preyer's reflex, weighing between 190 and 375 g, were used. The animals were anesthetized with intraperitoneal sodium pentobarbital (33 mg/kg body weight), relaxed with suxamethonium chloride, and artificially respirated through a tracheal cannula. Muscle relaxation was maintained by pancuronium bromide. Electrocardiography and heart rate were monitored in all animals throughout the experiment. The mean arterial blood pressure was recorded in some animals from a catheter inserted into the right carotid artery and connected to a blood pressure transducer. A heating pad around the body maintained the rectal temperature at 36°C to 38°C. Jugular vein cannulation was carried out for the administration of supplemental sodium pentobarbital, pancuronium bromide, and the agents tested. The animal's head was fixed in a dorsal position with a head-holder. The ES, in most animals on the left side, was exposed extradurally by the posterior occipital approach.[1-3,6] The sigmoid sinus was detached from the medial surface of the temporal bone. The ES was identified just behind the sigmoid sinus. A glass microelectrode inserted into the intermediate portion of the ES to measure the ESP was filled with 154 mmol/L sodium chloride because it has been reported that the ES has an electrolyte composition similar to that of the extracellular fluid.[3,7] A preliminary study of microelectrodes for the ESP measurement showed that a glass microelectrode filled with 154 mmol/L sodium chloride gave ESP values and ESP responses to canrenoate similar to those of one filled with 3 mol/L potassium chloride. A microelectrode with a tip diameter of 2 to 6 μm was used because it was more easily inserted through the tough walls of the ES. Connection of the microelectrode for the measurement of the ESP was made via silver–silver chloride to an amplifier with high input impedance of 10^{15} Ω (World Precision Instruments FD 223). The reference electrode was a silver–silver chloride electrode placed on the neck muscles. All experiments were carried out in an electrically shielded booth.

Drug Administration. Aldosterone (*d*-aldosterone, Sigma) was dissolved in ethyl alcohol and diluted in 5 mL of saline to make a concentration of ethyl alcohol of approximately 3%, which was intravenously infused for 5 minutes. Three-percent alcohol produced no change in the ESP (Table 1). An aldosterone antagonist, canrenoate (potassium canrenoate, Searle) dissolved in 4 mL of saline, was infused for 20 minutes with an infusion pump (Terumo STC-521) through a catheter inserted into the jugular vein. The canrenoate solution had a high potassium concentration. For example, a canrenoate solution of 300 mg/kg given to an animal weighing 300 g contained K^+ at a concentration of approximately 57 mmol/L. The infusion of a high-K^+ solution produced no change in the ESP (Table 1). Canrenoate was administered by a 20-minute infusion to make the influence of high potassium on the heart as small as possible.

Characteristics of Canrenoate. Like spironolac-

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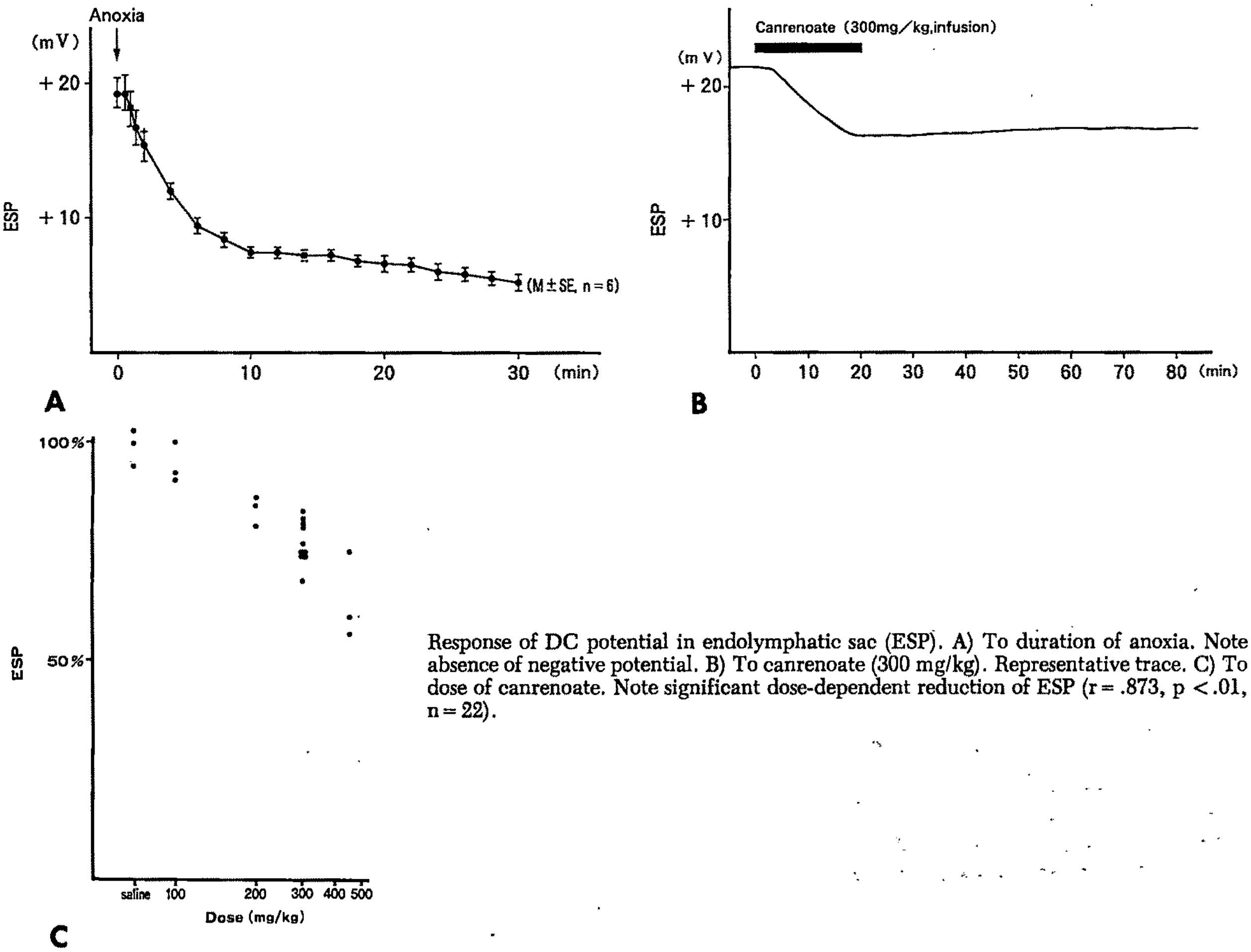

Response of DC potential in endolymphatic sac (ESP). A) To duration of anoxia. Note absence of negative potential. B) To canrenoate (300 mg/kg). Representative trace. C) To dose of canrenoate. Note significant dose-dependent reduction of ESP (r = .873, p < .01, n = 22).

tone, potassium canrenoate is a steroid derivative that is an indirect aldosterone antagonist. Spironolactone and potassium canrenoate are both metabolized to canrenone, which is an active aldosterone antagonist. Potassium canrenoate can be regarded as the potassium salt of one of the spironolactone metabolites.[8] Unlike spironolactone, potassium canrenoate is a water-soluble substance that can be administered parenterally.

Data Analysis. Values are presented as mean ± SEM. Student's *t* test was used to determine the statistical difference.

RESULTS

The mean ESP recorded was +19.4±1.2 mV (n = 26). The value of the ESP is comparable to that in previous reports.[1-3] The Figure (A) shows the response of the ESP to anoxia, which was produced by stopping the respirator. The ESP showed a rapid decrease for 5 to 6 minutes after the onset of anoxia. After that time the ESP gradually approached 0 mV. The ESP has no negative potential, unlike the DC potentials in the cochlea and vestibule. This finding is similar to that in previous reports.[1-3]

Aldosterone (1 mg/kg) induced no significant change in the ESP for 1 hour after the injection (Table 1). The injection of aldosterone (1 mg/kg) produced little change in the heart rate.

The Figure (B) shows a representative recording of the ESP in the 20-minute infusion of canrenoate (300 mg/kg). After the start of the infusion, the ESP began to gradually decline, and it reached a stable value at approximately 25 minutes. The ESP showed no remarkable recovery after the infusion was stopped. Canrenoate produced a significant decrease in the ESP (Table 1). The 20-minute infusion of canrenoate produced little change in the mean arterial blood pressure and heart rate in animals. The time taken to reach the minimum value of the ESP after the start of infusion of canrenoate was 22.0±1.9 minutes (n = 11). The infusion of physiologic saline and saline containing a high potassium concentration (50 mmol/L and 104 mmol/L) produced no significant change in the ESP (Table 1). The Figure (C) shows a significant dose-dependent reduction of the ESP in response to canrenoate.

Table 2 shows the difference in the ESP decrease between the following two groups: group 1, in which canrenoate (300 mg/kg) was administered, and group 2, in which canrenoate (300 mg/kg) was administered 60 minutes after pretreatment with aldosterone (1 mg/kg). There is no significant difference in the ESP value before infusion of canreno-

TABLE 1. EFFECT OF ALDOSTERONE AND ITS ANTAGONIST ON DC POTENTIAL IN ENDOLYMPHATIC SAC

Agents	*Infusion Time (min)*	*No. of Animals*	*ESP in mV (Mean ± SE)* Control	Experimental
Saline	20	5	20.2±2.0	20.1±1.9
Saline with 3% ethanol	5	5	20.3±1.7	19.2±1.5
Aldosterone 1 mg/kg	5	5	20.2±2.8	20.3±2.2
Saline with 50 mmol/L K^+	20	4	20.9±3.3	20.6±3.0
Saline with 104 mmol/L K^+	20	3	20.7±1.1	21.9±1.5
Canrenoate 300 mg/kg	20	11	19.5±2.2	15.1±1.6*

Experimental ESP value was measured at 60 minutes after start of infusion, except in animals given canrenoate.

ESP — DC potential in endolymphatic sac.

*Significant change ($p<.001$) in ESP amplitude between control and experimental groups.

TABLE 2. INFLUENCE OF ALDOSTERONE (1 MG/KG) PRETREATMENT ON CHANGE IN ESP INDUCED BY CANRENOATE (300 MG/KG)

Time After Start of 20-min Infusion (min)	*Relative ESP Amplitude (%, Mean ± SE)* Group 1 (n = 6)	Group 2 (n = 5)
0	100	100
10	89.6±3.1	93.4±3.9
20	79.4±2.5	83.8±4.9*
30	78.5±3.7	88.7±2.1†
40	79.3±3.3	94.7±2.9†
50	80.0±3.7	95.2±4.3†

Initial ESP for group 1, 21.4±3.7 mV, and for group 2, 19.2±1.7 mV.

ESP — DC potential in endolymphatic sac.

*Significant between groups 1 and 2 ($p<.05$).

†Significant between groups 1 and 2 ($p<.001$).

ate between both groups. In group 1 canrenoate decreased the amplitude of the ESP with no remarkable recovery at 50 minutes after the start of the infusion. In group 2 canrenoate decreased the ESP to a lesser degree than in group 1, and the recovery was observed after the infusion was stopped. The results demonstrate that pretreatment with a high dose of aldosterone attenuates the suppression of the ESP induced by canrenoate.

DISCUSSION

The present study confirms the finding of previous reports[1-3] that an anoxia-sensitive positive endolymphatic DC potential is recorded in the intermediate portion of the ES in the guinea pig. The amplitude of the ESP in the albino animals used in the present study is comparable to those of the previous reports in which pigmented animals were used.[1-3] The origin of the ESP is still unknown. However, the fact that the ESP is oxygen-dependent suggests the involvement of an active ion transport.

The present study showed that canrenoate, known as an aldosterone antagonist, suppresses the ESP and that aldosterone attenuates the effect of canrenoate on the ESP. Two major possibilities can be raised to explain the ESP change by canrenoate.

1. There may be an indirect effect of canrenoate on the ES, in which the ESP decrease results secondarily from the systemic effect produced by canrenoate. The possibility that the change in the circulatory system may produce the ESP reduction can be ruled out, because canrenoate infusion produced little change in the mean arterial blood pressure and heart rate. The possibility that the change in serum K^+ and Na^+ (an increased serum K^+ and a decreased serum Na^+) induced by the action of canrenoate on the kidney may cause a decrease in the ESP cannot be completely ruled out by the present results. However, an infusion of high-potassium solution induced no change in the ESP. Our previous studies have reported that loop diuretics (ethacrynic acid[3] and furosemide[9]), which are known to induce a decreased serum Na^+, produce no significant change in the ESP at a high dose (100 mg/kg intravenously). The possibility that changes in blood level of the organic substances produced by canrenoate administration may result in a decrease in the ESP cannot be ruled out. It is possible that aldosterone may attenuate the effect of canrenoate on the ESP change via the amelioration of action of canrenoate on other organs such as the kidney.[4,5]

2. There may be a direct effect of canrenoate on the ES. The possibility that canrenoate may decrease the ESP by suppressing the action of aldosterone on the ES can be raised. The previous report[3] favors the possibility that Na^+ may be actively pumped out of the ES, that the ESP may be involved in Na^+ transport in the ES, and that Na^+ transport in the ES may play an important role in the longitudinal flow of endolymph in the inner ear. Aldosterone is found to stimulate sodium absorption in certain mammalian epithelia such as cortical collecting tubule[4,5] and colon.[10,11] It is tempting to speculate that aldosterone may regulate the longitudinal flow of the endolymph through stimulation of Na^+ transport in the ES. However, the finding that aldosterone failed to produce an increase in the ESP may argue against this possibility. The failure of the ESP to be changed by aldosterone might be accounted for by the possibility that a physiologic aldosterone blood level may be enough to maintain the normal ESP in the normal animal. To test this possibility the same experiment must be performed in adrenalectomized animals. Previous experiments on endolymphatic hydrops formation[12] have revealed that after ES obliteration, it takes at least 1 day for endolymphatic hydrops to form. This finding suggests that the longitudinal endolymph flow rate is small. This hypothesis has been supported by a recent study involving measurement of longitudinal endolymph flow rate.[13] If aldosterone regulated the longitudinal endolymph flow in the

ES, a large number of aldosterone receptors would not be needed to play a role in the ES, since the longitudinal endolymph flow rate is small.

Further study is necessary to clarify the mechanism underlying the ESP decrease caused by canrenoate.

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HEMANGIOMA OF THE TEMPORALIS MUSCLE

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A rare case of an intramuscular hemangioma of the temporalis muscle is reported. The clinical examination, carotid arteriogram, computed tomographic scan, and aspiration cytology suggested the vascular nature of the tumor, but an exact diagnosis could only be made after histopathologic examination. Temporary occlusion of the ipsilateral external carotid artery and subperiosteal dissection permitted complete, wide excision without much bleeding.

KEY WORDS — head and neck neoplasms, hemangioma.

INTRODUCTION

Intramuscular hemangiomas (IMHs) are uncommon tumors of vascular origin, and because of their deep location, their paucity of typical clinical features, and the average clinician's unfamiliarity with their clinical and radiographic presentation, more than 90% are misdiagnosed preoperatively.[1-4] Arteriography and computed tomography (CT), although helpful in defining the extent of the lesion, offer no certitude in the diagnosis.[5,6] Aspiration cytology, likewise, can point to the vascular origin of the tumor but may not disclose its exact nature. Open biopsy, although feasible, is rarely contemplated because of the tumor's deep location and the danger of bleeding.[2]

Management of IMH must be individualized depending upon the tumor location, accessibility, and cosmesis.[3] The published English literature contains only four cases of IMH of the temporalis muscle, cited from the European literature.[7-10] We report another case in the present communication. We were unaware of the exact nature of the tumor until histopathologic confirmation. Its rare location, difficulty in the preoperative diagnosis, its successful treatment, and lack of such a case report in the last three decades make this case worthy of presentation.

CASE REPORT

A 21-year-old man, otherwise healthy, presented with the complaint of a swelling in the left temple that had been gradually increasing in size with occasional pain for the last 3 months. There was no history of trauma. Clinical examination revealed a smooth, round, firm, pulsatile, nontender and noncompressible swelling with a well-defined edge measuring 5 cm in diameter located under or inside the temporalis muscle. The overlying skin was normal, and the superficial temporal artery was found coursing over the swelling. Pressure over the left common carotid artery caused pulsations to cease, but there was no palpable thrill or audible bruit. Findings on the general physical, cardiovascular, otolaryngologic, and neurologic examinations were unremarkable. No other swelling was palpable anywhere in the body, and the regional lymph nodes were not enlarged. Clinically, the possibility of a cirsoid aneurysm or a muscle tumor was considered.

Findings on the differential blood count and radiography of the chest and skull were normal. The carotid arteriogram showed a faint tumor blush of abnormal arteries along with enlargement of the internal maxillary artery (see Figure, A). The plain CT scan of the head showed an enlarged left temporalis muscle suggesting an isodense mass within it (see Figure, B). Injection of contrast produced homogeneous enhancement of the whole muscle (see Figure, C). No erosion of the temporal bone or intracranial extension was noted. Fine needle aspiration yielded blood, and cytologic examination showed spindle-shaped cells with hyperchromic nuclei and endothelial cells offering a presumptive diagnosis of a vasoformative tumor. With this diagnosis, the patient was operated on.

First, the left external carotid artery was exposed in the neck and a tape was passed around it. A question mark–shaped incision was made from the frontotemporal crest to the zygomatic arch, and a skin flap was reflected from the underlying temporal fascia. The temporalis muscle along with the fascia was raised subperiosteally from the underlying bone. Its insertion into the coronoid process was also raised, and the muscle was excised en masse. One large and a few smaller arterial feeders required coagulation during dissection of the anteroinferior part of muscle. The wound was closed in layers and a vacuum drain was maintained for 48 hours.

Gross inspection of the cut specimen showed a whitish, well-circumscribed tumor, containing empty spaces, within the muscle. Histopathologic exam-

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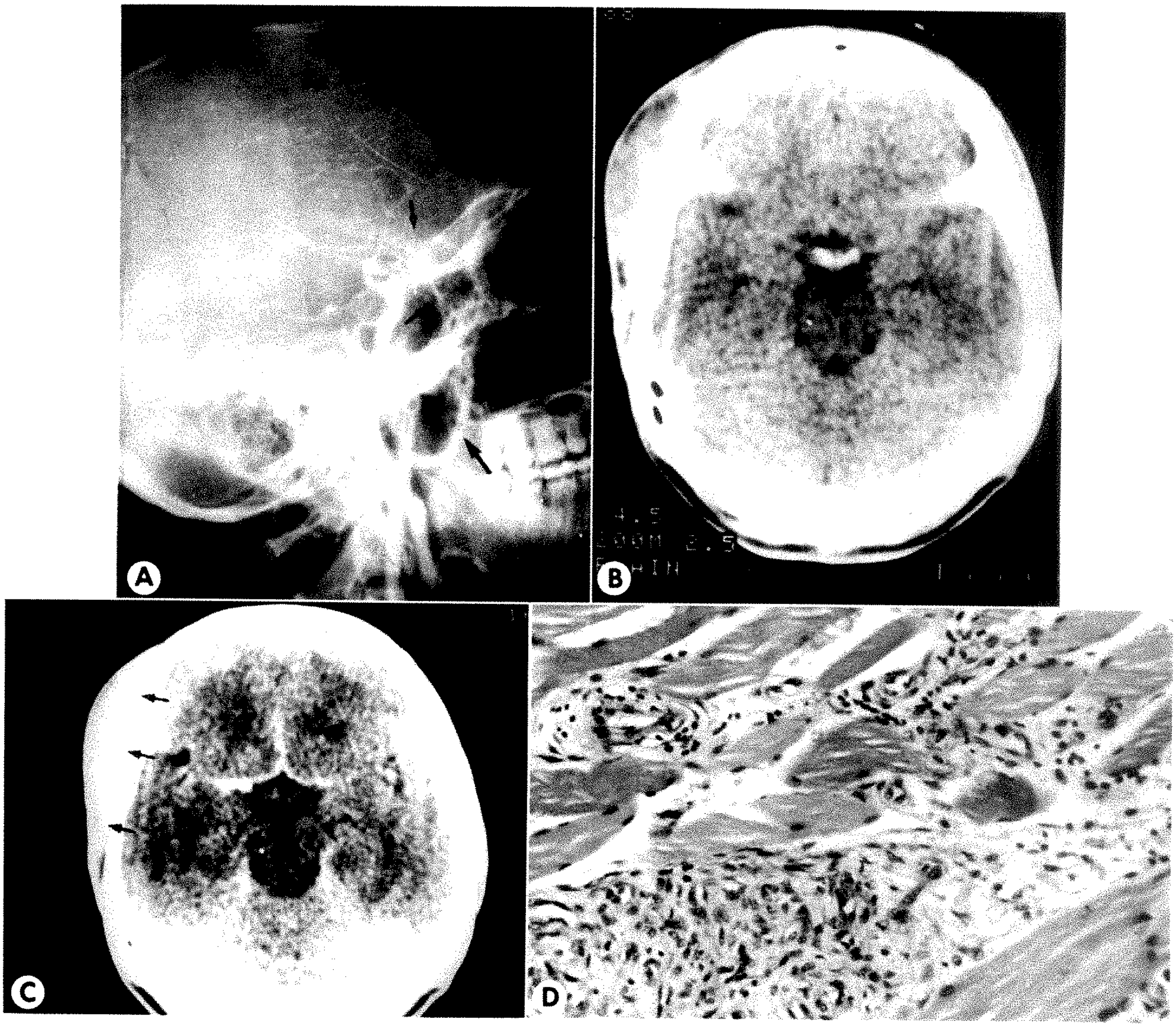

Hemangioma of temporalis muscle. A) Carotid arteriogram showing enlarged caliber of internal maxillary artery (large arrow) and faint tumor blush of abnormal vessels (small arrows). B) Plain computed tomograph showing left temporal enlargement to be muscle. C) Contrast-enhanced computed tomograph showing uniform enhancement of temporal enlargement to be muscle (arrows). D) Photomicrograph showing tumor composed of small capillaries with prominent endothelial cells (H & E, original x160). Muscle fibers are separated by proliferating capillaries.

ination showed the tumor to be composed predominantly of small capillary-size blood vessels lined by plump endothelial cells. In most of the areas a well-defined lumen was seen. In some areas the tumor had a solid appearance. A few large vessels were present. Characteristically, the tumor extended between individual muscle fibers, giving a pseudoinfiltrative appearance (see Figure, D).

Follow-up 6 months later revealed a hollow in the left temporal fossa, for the correction of which the possibilities of a fat graft or implant have been discussed with the patient.

DISCUSSION

In the large constellation of varieties of soft tissue tumors of vascular origin, IMH constitutes only 0.8% of all benign vascular tumors.[1] These tumors present as enlarging soft tissue masses of less than a year's duration, with or without pain. Eighty percent to 90% occur before the age of 30 years, and both sexes are afflicted with equal frequency. The skin and subcutaneous tissue are not involved and are freely mobile. Symptoms and signs to indicate their vascular nature, ie, discoloration of overlying skin, visible pulsations, and audible bruit, are rarely seen. The rarity of the lesion causes it to be ignored in a differential diagnosis, and it is commonly confused with benign or malignant neoplasms of the muscle, neurofibroma, or aneurysm. More than 90% of these lesions are misdiagnosed.[2,10-12] Plain x-ray films, angiography, and CT scan may not be specific for this tumor.[4]

At arteriography, these lesions are highly vascular, with early venous runoff. In addition, they demonstrate feeders. The vessels are oriented parallel to one another in a striated pattern between the fascicles of muscle, suggesting benignancy.[3,12] Arteriography may fail to demonstrate an IMH when it is supplied by small arteries with slow blood flow.[2,6] The feeding vessels to an IMH usually are few and are larger in caliber than adjacent arteries.[2,5]

On plain CT scan, the density of the hemangioma is similar to that of muscle. Injection of contrast suggests a vascular mass within the muscle, but does not allow differentiation between the lesion and muscle or surrounding tissues.[6,13] It may demonstrate or exclude bony erosion, major vessel involvement, and intracranial extension.[14] However, dynamic CT and magnetic resonance imaging are reported to provide excellent delineation and confirmation of the diagnosis.[4,6,13,15] Aspiration of blood and cytology may be diagnostic,[2] but the exact nature of the tumor was not disclosed in the present case.

The most accepted theory of pathogenesis is that it is a congenital mass of abnormal embryonic sequestration.[8] Trauma may play an important role, since a history of trauma is present in 20% of cases.[16] The IMHs are best classified into small vessel (capillary), large vessel (cavernous), and mixed types. It may not be possible to simply classify them, because they are types of the same pathologic spectrum. Capillary types have a greater predilection for the head and neck musculature. The histologic characteristics of the present case were typical; mitotic activity, intraluminal capillary tufting, and a pseudoinfiltrative pattern do not indicate malignancy.[11,12,17]

Although any muscle can be affected, the majority of IMHs occur in the lower limbs, particularly the muscles of the thigh.[12] Eight to fifteen percent of IMHs arise in the head and neck musculature.[3,8-11] There are only 74 cases of IMHs of the head and neck musculature reported in the literature through 1985. The masseter muscle is the commonest site, followed by the trapezius and sternomastoid.[3] Involvement of the temporalis muscle is cited in only four cases.[7-10] The age of the patients in these cases ranged from 5 months to 37 years. A history of trauma was present in three cases. These lesions were often mistaken for dermoid cysts or aneurysms.[7,8]

Most cases require surgical removal. The best treatment is aimed at wide excision with resection of muscle well beyond the tumor.[3,16] Eighteen percent of these lesions recur, and minor feeders are responsible for this recurrence. In order to reduce recurrence and the risk of intraoperative hemorrhage, knowledge of the size and extent of the lesions and feeder vessels beforehand is important.[2,11,12,17] Ligation or embolization of feeder arteries causes visible shrinkage of tumor and reduces hemorrhage and vascularity of surrounding structures, making excision easier.[5,14] Temporary occlusion of the ipsilateral external carotid artery reduces blood flow by 50%.[18] This maneuver, along with dissection well beyond the tumor (ie, superficial to temporalis fascia and subperiosteal deep to muscle) and preoperative visualization of feeders, provided a bloodless field and better control of feeders, enabling complete excision of the lesion without difficulty in the present case.

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IMAGING CASE STUDY OF THE MONTH

COMPUTED TOMOGRAPHIC DIAGNOSIS OF SEPTIC LATERAL SINUS THROMBOSIS

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INTRODUCTION

Septic thrombosis of the lateral sinus is usually established on clinical grounds in the presence of an otogenic infection. The altered clinical picture of this condition in the era of antibiotics may be misleading and therefore additional examinations are required for early diagnosis and treatment of this serious complication. Computed tomography (CT) today may replace angiography in detecting dural venous sinus thrombosis. We present a case of septic lateral sinus thrombosis (LST) secondary to a masked mastoiditis, accurately diagnosed by CT.

CASE REPORT

A 12-year-old boy was referred to the Department of Otolaryngology with fever, chills, headache, vomiting, and left-sided otalgia after 1 week of treatment by amoxicillin for an acute left-sided otitis media. He had a history of recurrent middle ear infections and had had ventilating tubes inserted in both ears at the age of 6.

On admission, he was febrile (40°C) and confused. Otoscopy revealed a hyperemic and edematous left ear canal by which an intact tympanic membrane with loss of landmarks was visualized. No discharge from this ear was found. Tenderness in the left postauricular area and along the left sternocleidomastoid muscle was present. The rest of the findings on otolaryngologic examination were normal. No unusual neurologic signs were detected. On fundoscopy, bilateral papilledema was observed.

The laboratory investigations revealed an elevated sedimentation rate of 50/90 mm, hemoglobin of 8.1 g/dL, and a white blood cell count of 26,000 mm^3 with a shift to the left. Radiographs of the ears showed a poorly pneumatized left mastoid with an erosive lesion of the left periantral area suggestive of cholesteatoma. Contrast-enhanced cranial CT showed in addition an erosion in the posterior bony wall of the left antrum. Posterior to it, an enhancing ring lesion with a low-density center was seen in serial slices at the anatomic site of the apparently dilated left lateral sinus (see Figure). Accordingly, ceftazidime 100 mg/kg daily was initiated and mastoidectomy was indicated.

At operation, the mesotympanum, facial recess, aditus, and antrum were found to be filled with cholesteatoma. The incus and the stapes were partially eroded. The air cells of the mastoid were filled with purulent exudate, and a perisinus abscess was present. Granulation tissue covered the osteitic wall of the lateral sinus, and the sinus itself was not compressible. The lateral sinus was incised longitudinally and pus and thrombus were evacuated. A radical mastoidectomy was performed. Culture specimens from the perisinus abscess and infected thrombus were sterile.

Postoperatively, the patient developed mild meningeal signs that resolved during the second week of hospitalization.

DISCUSSION

Lateral sinus thrombosis is rare today, but still is a life-threatening condition.[1] It almost always arises from an inflammatory lesion in the nearby mastoid or middle ear. The wide use of antibiotics has significantly reduced the number of complications of acute otogenic infections, and LST is at present most commonly found in neglected chronic ear disease[1] and during the course of low-grade infections of the middle ear cleft.[2] The latter condition, known also as masked mastoiditis,[3] follows an insidious course until intracranial complications develop, as observed in the present case. Interference with the normal ventilation of the mastoid air cells by mucosal changes or cholesteatoma in the aditus ad antrum has been suggested as the likely pathogenesis of this condition. By the nature of mastoid-colonizing flora at low oxygen saturations, the production of pus is minimal and the resulting osteitis may be indolent. The otoscopic examination may reveal normal findings or only minimal abnormalities. Therefore, these patients may escape medical attention.

The diagnosis of LST is usually established on clinical grounds.[1] Fever with or without a spiking

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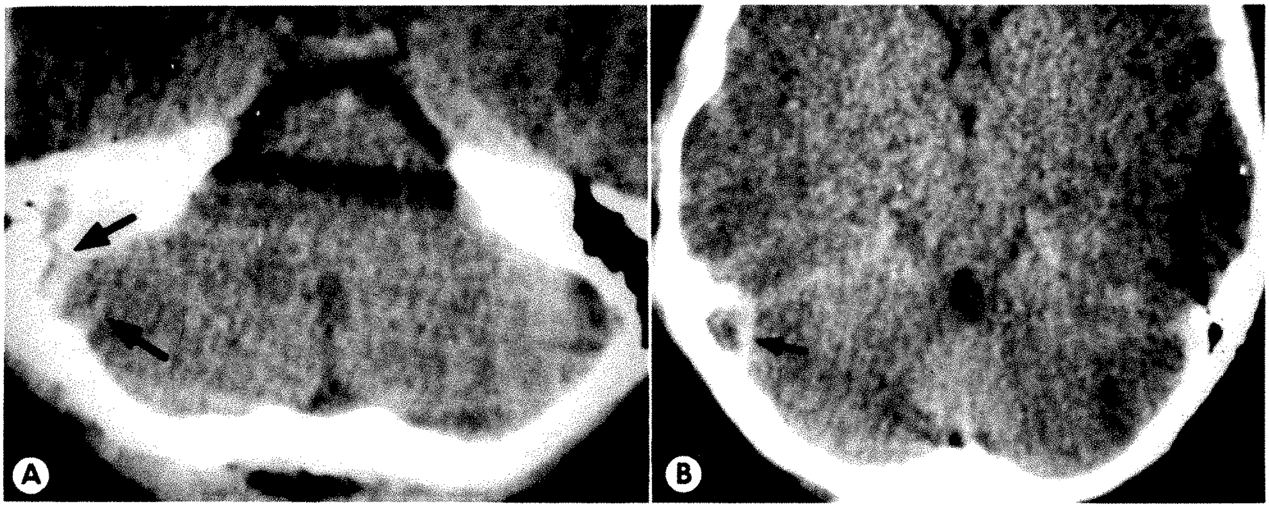

Axial contrast-enhanced computed tomograms of posterior fossa. A) Erosion of posterior aspect of mastoid antrum (upper arrow). Posterior to it, contrast-enhanced ring lesion located in lateral sinus is seen (lower arrow). Radiodensity of whole middle ear and most of antrum is evidence of cholesteatoma. B) At higher level, contrast-enhanced ring lesion in lateral sinus is more prominent (arrow; compare to opposite side).

curve, chills, otalgia, tenderness to percussion over the mastoid emissary vein, deteriorating mental status, papilledema, and leukocytosis are common but not pathognomonic features. Less commonly, elevated cerebrospinal fluid pressure, anemia, or emaciation may also occur. Occasionally, remote septic conditions such as pneumonia[4] or superior vena cava syndrome[5] are the presenting symptom of LST. Besides the rarity of LST, the nonspecificity of the signs and symptoms and the masking effects of antibiotic therapy[1] make the diagnosis difficult. Routine radiographs of the mastoids show only an inflammatory temporal bone disorder. Vascular studies (carotid angiography and jugular venography) are highly specific in the recognition of LST, but are invasive procedures carrying the risk of dislodging the thrombus.[1] More recently, digital subtraction angiography has gained importance as a relatively low-risk procedure in the recognition of dural sinus thrombosis. Dynamic rapid sequential radionuclide brain scanning has also been helpful in evaluating patients with suspected LST.[6] Computed tomographic scanning is at present the most widely used imaging investigation for intracranial disorders. Contrast-enhanced cranial CT has proved effective in detecting many, but not all, venous dural sinus thromboses.[7] Segall et al[8] reported that CT filling defects in venous sinuses cannot be appreciated on standard window scans. The differentiation between contrast-enhanced venous vessels and the adjacent bony structures is feasible only on high-resolution scans with an expanded window width.

The role of CT in detecting LST has been documented in isolated case reports.[7,9] Multiple intraluminal filling defects and nonvisualization of the lateral sinus on contrast-enhanced CT were reported as positive signs for LST.

In our case, investigated with conventional cranial CT, the enhancement of the sinus walls in serial slices was consistent with the diagnosis of LST. The lateral sinus lies within a duplication of the dura mater. In the presence of an adjacent and persistent infection (perisinus or extradural abscess), the dural outer wall of the sinus may become inflamed[10] and develops a circumscribed perisinus meningitis. Subsequently the infectious inflammatory process reaches the intima of the venous sinus and gives rise to phlebitis, a mural thrombus, and finally an obliterating thrombus. The thrombus formed within the lumen of the sinus may present different attenuations according to its developmental stages. Fresh clots in the sinus appear as high density without contrast enhancement. Because of degradation of the hemoglobin within days, the intraluminal thrombus changes to low density, and this is better demonstrated by contrast-enhanced high-resolution CT. The CT appearance of LST in axial slices is an enhanced ring lesion, the opacification being the result of contrast absorption by the perisinus meningitis present.

Because of the nonspecific signs and symptoms of the disease and the masking effect of antibiotics, the diagnosis of LST is difficult. Delay in its diagnosis and treatment often results in high morbidity and mortality rates.[1] Therefore, CT demonstration of an inflammatory perisinus meningeal reaction is of utmost importance in the recognition of this life-threatening condition.

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PATHOLOGY CONSULTATION

UNDIFFERENTIATED CARCINOMAS OF SALIVARY GLANDS

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Undifferentiated carcinomas of salivary glands are those epithelial malignancies whose light-optic histopathologic features are not sufficient to place them in other defined classes of carcinoma. They are ultrastructurally heterogeneous and can manifest neuroendocrine differentiation. With or without the latter, the carcinomas are biologically high-grade and rank with salivary duct and high-grade mucoepidermoid carcinomas in terms of morbidity and mortality.

An undifferentiated carcinoma of salivary glands is defined as one without enough distinguishing light-optic features to allow placement in another classification of salivary gland malignancy.[1] That this seemingly exclusive definition has not been uniformly applied is evinced by a reported range of incidence from 1% to 30% of all malignant salivary gland tumors.[2] Hui et al[2] have suggested at least three reasons for the wide spread in estimated frequency: 1) failure to exclude metastases, notably Merkel cell and metatypical basal cell carcinomas, to salivary glands (almost exclusively the parotid gland), 2) inclusion of otherwise classifiable primary carcinomas, eg, high-grade adenoid cystic carcinomas and carcinomas ex pleomorphic adenoma, and 3) inappropriate use of "undifferentiated" as a qualifying diagnostic adjective for nonmalignant salivary tumors such as basaloid monomorphic adenomas and the rarely occurring embryomas. It is likely, once such lesions are culled, that undifferentiated carcinomas account for less than 1% or 2% of all salivary gland tumors of the *major* salivary glands[3] and perhaps an equal percentage from minor salivary tissues.

Undifferentiated carcinomas of salivary origin are preponderantly "small cell" (see Figure; A,B), indicating a cell diameter of 30 μm or smaller but occasionally up to 60 to 90 μm.[2-6] Anaplastic carcinomas with large, "monstrocellular" constituents can usually have their lineage traced back to other high-grade carcinomas, most often ductal carcinomas.[7]

Controversy usually attends rare or unusual neoplasms, and the undifferentiated carcinomas of salivary glands are not exceptions. Contentions center about the cell(s) of origin and biologic behavior, especially as compared to small cell carcinomas of the lung.[3,8]

It is estimated that 4% of all small cell carcinomas arise in extrapulmonary tissues.[3] In the head and neck, besides the major salivary glands (preponderantly the parotid gland), the carcinomas have been reported as originating in the larynx, sinonasal tract, and the upper digestive tract (oral cavity to cervical esophagus). Primary undifferentiated small cell carcinomas of the major salivary glands are considered to arise from ductal stem cells with a multidirectional capacity.[2-4,9] Less conviction obtains for the undifferentiated carcinomas outside of the major salivary glands, where a salivary tissue origin either cannot be well established or is excluded.[3,8,10]

The small cell undifferentiated salivary carcinomas have often been diagnostically characterized by their growth patterns, eg, solid or trabecular, or by borrowing terms from pulmonary pathology, eg, "oat cell carcinoma."[8] The latter has carried with it prognostic and therapeutic implications extrapolated from lung carcinomas, lacks interobserver precision, and even among pulmonologists is being redefined.[11] It should be avoided as a diagnosis for undifferentiated carcinomas of the salivary tissues.

It is clear from ultrastructural examination of undifferentiated carcinomas of the major salivary glands that they are not a homogeneous group.[2,9,12] Some will be so undifferentiated that they exhibit no distinguishing electron-optic findings. A ductal or epidermoid appearance, not noticeable by light-optic study, will be present in others, and a number of these will also manifest neuroendocrine differentiation (see Figure, C).[2,12]

Of 52 reported undifferentiated small cell major salivary gland carcinomas, 40 were studied with the electron microscope.[2,12] Eleven (27.5%) manifested secretory granules of a type to point to neuroendocrine differentiation. An immunocytochemical alternative to ultrastructural definition of neuroendocrine differentiation (chromogranin and neuron-specific enolase reactivity) is acceptable, but is not completely specific and is dependent on secretory granule density (see Figure, D). The neuroendo-

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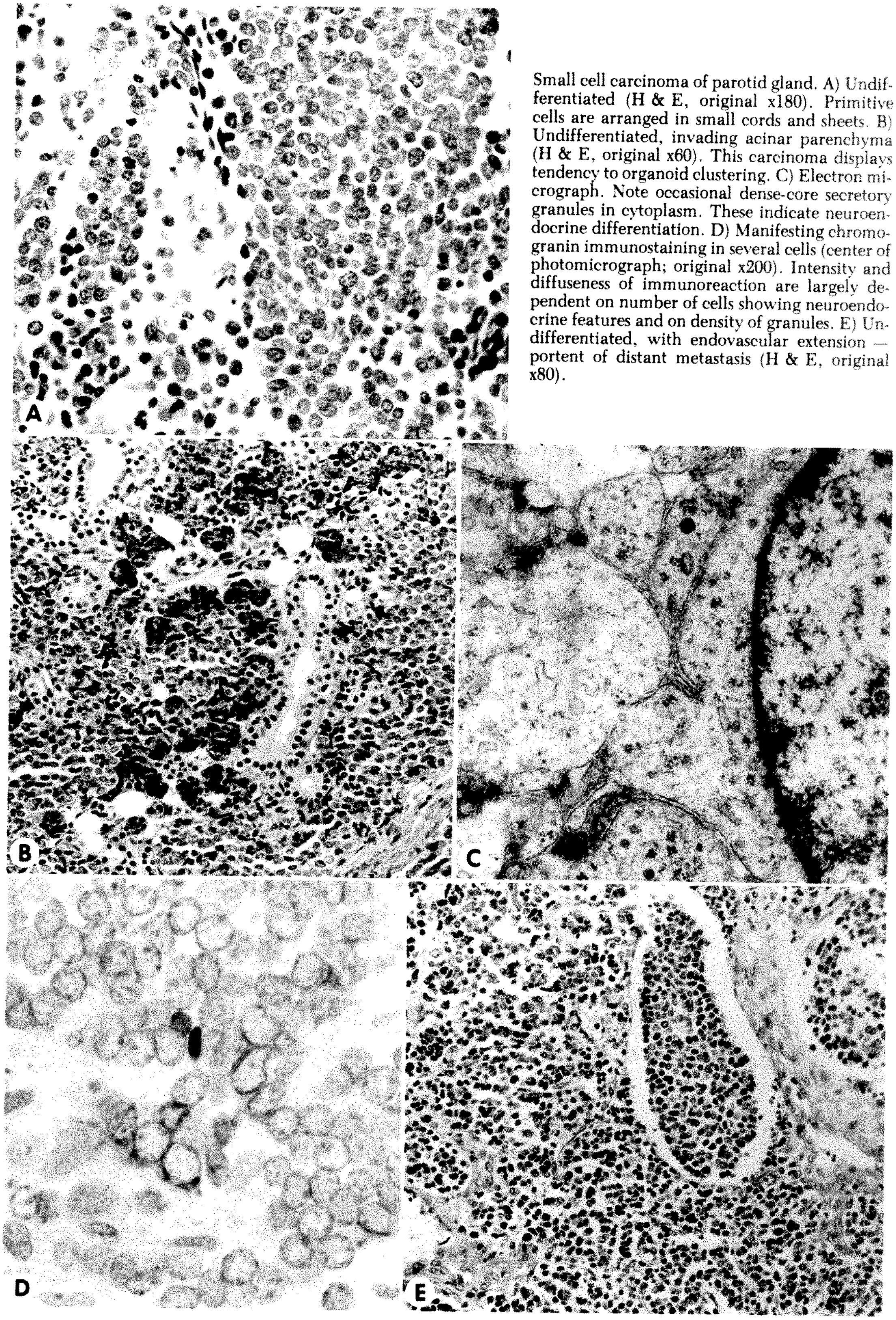

Small cell carcinoma of parotid gland. A) Undifferentiated (H & E, original x180). Primitive cells are arranged in small cords and sheets. B) Undifferentiated, invading acinar parenchyma (H & E, original x60). This carcinoma displays tendency to organoid clustering. C) Electron micrograph. Note occasional dense-core secretory granules in cytoplasm. These indicate neuroendocrine differentiation. D) Manifesting chromogranin immunostaining in several cells (center of photomicrograph; original x200). Intensity and diffuseness of immunoreaction are largely dependent on number of cells showing neuroendocrine features and on density of granules. E) Undifferentiated, with endovascular extension — portent of distant metastasis (H & E, original x80).

crine features, regarded as an intrinsic feature of the cells rather than misplaced neural crest cells, have been considered as perhaps modifying biologic behavior.[2,3] Hui et al[2] have concluded otherwise. Their data show that *none* of the cytologic or ultrastructural findings in undifferentiated major salivary gland carcinomas have a significant singular bearing on patient outcome. The most significant factor in prognosis is the size of the primary carcinoma, with neoplasms 4 cm or larger having a particularly ominous prognosis. Ten of 16 patients studied by Hui et al[2] died of their carcinoma, with a mean survival time of 31 months. Distant metastases (see Figure, E) occurred in 9 of the 10 patients. Local recurrences and metastases to regional lymph nodes were frequent — nearly 60% in either instance.

Adherence to the World Health Organization[1] definition of undifferentiated salivary gland carcinoma serves to place these neoplasms in classification schemes and perhaps allows for epidemiologic studies. The undifferentiated carcinoma with lymphoid stroma with its ethnic, geographic, and Epstein-Barr virus relationships is a case in point.[13] Other than that, however, it should be recognized only as a high-grade malignancy with a biologic course and lethality very similar to that of other high-grade carcinomas of salivary glands, eg, salivary duct, solid adenoid cystic, and high-grade mucoepidermoid carcinomas.

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LARYNGEAL DYSTONIA: A SERIES WITH BOTULINUM TOXIN THERAPY

ANDREW BLITZER, MD, DDS MITCHELL F. BRIN, MD

NEW YORK, NEW YORK

Laryngeal dystonia is a syndrome characterized by action-induced, involuntary spasms of the laryngeal muscles. Most patients have involvement of the adductor laryngeal muscles producing uncontrolled spasms during phonation, and a "strain-strangle" speech pattern commonly termed "spastic dysphonia." Other patients have involvement of the abductor muscles producing "whispering dysphonia." Rare patients have paradoxical vocal cord motion during respiration with adductor spasms on inspiration. Over the past 5 years we have used botulinum toxin (BOTOX) to treat more than 200 patients with laryngeal dystonia. This group includes patients with adductor involvement (phonatory dystonia, recurrent laryngeal nerve section failure, respiratory dystonia) and those with abductor involvement (whispering dystonia). Patients received benefit within 24 to 72 hours, with sustained improvement for 2 to 9 months with an average of 4 months. Patients improved to an average of 90% of normal function. Clinically significant adverse effects included extended breathy dysphonia and mild choking on fluids. BOTOX has become our treatment of choice for dystonic conditions of the larynx.

KEY WORDS — botulinum toxin, laryngeal dystonia, spastic dysphonia.

Laryngeal dystonia is a neurologic disorder of central motor processing characterized by action-induced spasms of the vocal cords. The spasms are poorly controlled by the patient, and the symptoms are exacerbated by stress. These spasms produce a clinical voice syndrome often termed spasmodic dysphonia (SD) or spastic dysphonia, which is characterized by a choked, constrained voice pattern with breaks in vocalization.[1,2] In addition, the voice pattern may also be tremulous with inhalation phonation, harshness, and audible grunts. In addition to the adductor form of laryngeal dystonia, approximately 10% of patients will present with the abductor form. In this form of phonation, the cords will have a spasmodic motion of the posterior cricoarytenoid (PCA) muscles, producing a breathy voice. The history of observations of SD has previously been reported.[2-8] Our group and others[9-12] have linked SD to dystonia, a central nervous system disorder. Dystonia may manifest itself in other focal and segmental presentations, including blepharospasm (forced, involuntary eye closure), oromandibular dystonia (face, jaw, or tongue involvement), torticollis (twisting of the neck), and writer's cramp (action-induced dystonic contractions of the hand muscles).[13-16] Laryngeal dystonia may present focally or in association with other dystonic movements.

Vocal analysis of the adductor SD patients reveals harshness, usually a tremor, inappropriate pitch or pitch breaks, groaning, breathiness, and glottal fry.[17,18] The voice arrests come from hyperadduction of the true and false vocal cords. Some of the patients with tremor have synchronous involvement of the pharynx, face, masticatory muscles, etc.[19,20] The abductor SD patients were described by Aronson et al[10] in 1968 as a group with a whispering dysphonia or aphonia. This may be the earliest report of the true abductor SD. Many of these patients may be misdiagnosed as having a vocal cord paralysis.

Our electromyography (EMG) data also showed 17% of patients with enlarged potentials, as well as 11% with polyphasic potentials.[9,21] This finding is indicative of some reorganizational activity, perhaps denervation and reinnervation.

In addition we have identified two other variations of presentation. The term compensatory abductor dysphonia refers to those patients with such severe adductor spasms that they voluntarily produce a breathy voice by not contracting their vocal cords in order to prevent the spasms and the broken speech pattern. Patients with compensatory adductor dysphonia are those severe abductors who try to prevent the breathiness by tightly contracting their vocal cords.[1]

Psychotherapy, speech therapy, and biofeedback are generally unsuccessful methods of treating SD. Recurrent laryngeal nerve section has a long-term success rate of about 36%,[22] with continued vocal cord paralysis. We have postulated[20] that this failure rate is related to hyperfunction of the opposing hyperfunctional dystonic muscle, which usually exaggerates the dystonic symptoms. Our series[1] has shown poor results of treatment of adductor dystonia with medication, although there was a 33% response rate in the abductor type. We therefore established a program of treatment of laryngeal dystonia with botulinum toxin (BOTOX) injections.

From the Departments of Otolaryngology (Blitzer) and Neurology (Brin) and the Dystonia Clinical Research Center (both authors), Columbia-Presbyterian Medical Center, New York, New York. Supported in part by a grant from the Dystonia Medical Research Foundation.

Presented at the meeting of the American Laryngological Association, Palm Beach, Florida, April 28-29, 1990.

REPRINTS — Andrew Blitzer, MD, DDS, Dept of Otolaryngology, Columbia-Presbyterian Medical Center, 630 W 168th St, New York, NY 10032.

METHODS

CLINICAL DATA

This study (approved by our Institutional Review Board) consists of a group of 260 primary and 60 secondary laryngeal dystonia patients, of whom 210 patients had the presumptive diagnosis of SD (adductor or abductor laryngeal dystonia) when referred. Patients were evaluated with a detailed history and physical examination including direct fiberoptic laryngoscopy with video recording, a complete neurologic examination, and laryngeal EMG; some had brain stem audiometric evoked response and magnetic resonance imaging scans. In questionable cases, the videotapes were reviewed to confirm the diagnosis. Patient data are stored in a Foxbase data base.

Initially we only invited patients who had previously failed treatment with pharmacotherapeutic agents. BOTOX has been so successful as compared to other modalities, with few clinically significant side effects, that we began to offer BOTOX as primary therapy. We also have offered BOTOX therapy to patients who have failed surgical therapy (recurrent laryngeal nerve section and anterior commissure release procedures), patients with abductor laryngeal dystonia, and patients with dystonic respiratory laryngeal dysrhythmias.

INJECTION TECHNIQUE

Adductor. Each patient had injections that were individualized with doses of 1.25 U to 3.75 U. Injections were given percutaneously with EMG guidance as we have previously reported.[23]

Abductor. The first abductor patient was initially treated with BOTOX via a direct laryngoscopy and injection into the PCA muscle. This was not possible to do with EMG control, and besides the patient discomfort, very little improvement was noted. We next began EMG-guided percutaneous injection. The larynx is manually rotated away from the side of intended injection and the hollow EMG needle with syringe is placed posterior to the posterior edge of the thyroid lamina. The needle is advanced to the cricoid cartilage and then moved out under EMG guidance to the optimum position in the PCA muscle.

RATING

Patient's voices were scored in a nonblinded fashion by means of a subjective rating scale estimating the percent of normal speech, with 0% representing no speech or full disability and 100% representing normal speech. Patients scored themselves before each injection, and a videotaping and voice recording were performed. In addition, the physicians made a similar rating and the most conservative rating was recorded and used as the percent improvement in all cases. Patients kept diaries of vocal function, noting the time of onset of vocal weakness, peak weakness, duration of breathy hypophonia, duration and severity of choking with liquids, and any other notable events. No correlation was made between the observed improvement and vocal cord paralysis, since with our technique, paralysis is very rare. Postinjection EMG studies were performed on the 2-week follow-up visit in a limited number of patients early in our study. The studies were not carried out in all patients since they did not appear to have direct clinical relevance.

DYSTONIA AT COLUMBIA-PRESBYTERIAN MEDICAL CENTER

	Laryngeal Dystonia (N = 320)		*All Dystonia (N = 1,926)*	
	Primary	*Secondary*	*Primary*	*Secondary*
N	260 (81%)	60 (19%)	1,356 (70%)	570 (30%)
F	152 (58%)	36 (60%)	813 (60%)	326 (57%)
M	108 (42%)	24 (40%)	543 (40%)	244 (43%)
F:M	1.4	1.5	1.5	1.3
Jewish	60 (23%)	13 (22%)	325 (24%)	112 (20%)
Non-Jewish	200 (77%)	47 (78%)	1,031 (76%)	458 (80%)
J:NJ	0.30	0.28	0.32	0.25
Positive family history	44 (17%)	5 (8%)	248 (18%)	48 (8%)
Focal	168 (65%)	15 (25%)	770 (57%)	168 (30%)
Segmental cranial	43 (17%)	6 (10%)	191 (14%)	55 (10%)
All segmental /hemidystonia	70 (27%)	18 (30%)	431 (32%)	203 (36%)
Generalized	20 (8%)	23 (38%)	138 (10%)	138 (24%)

RESULTS

CLINICAL CHARACTERISTICS

Laryngeal Dystonia Data. Of the 1,926 cases of dystonia registered at the Dystonia Clinical Research Center, 320 cases (16.6%) had vocal involvement. Of these 320 patients, 260 (81%) had primary dystonia and 60 (19%) had secondary dystonia (see Table). Of the primary group, 152 (58%) were female and 108 (42%) were male. This is very similar to the 60% female/40% male ratio found in the entire group of primary dystonias. The Jewish/non-Jewish ratio for primary laryngeal dystonia was 23%/77%, which is consistent with the 24%/76% found in the entire primary dystonia group.

In the group of 320 patients with laryngeal dystonia, 270 (84.4%) had adductor vocal involvement ("spastic dysphonia"); 47 (14.6%) had abductor vocal involvement ("whispering dysphonia"); and 3 (1%) had adductor breathing dystonia. The average age at onset of SD patients was 38. The three patients with laryngeal adductor breathing dystonia were 27, 55, and 56 years of age at onset. Of interest was the fact that 27 patients of the primary dystonia group (10.4%) had laryngeal involvement first and then went on to have involvement of another neuromuscular system. The importance of family history is illustrated by the fact that 44 of the 260 (17%) patients who had primary laryngeal dystonia had a family history of dystonia.

BOTULINUM TOXIN THERAPY

Adductor Laryngeal Dystonia. Of the 320 cases of laryngeal dystonia recorded in our data base, we have injected 210 patients since April 1984. At the inception of our study, there were no previous guidelines for laryngeal BOTOX injections and therefore our dose schedule was empiric. Recognizing that the vocalis-thyroarytenoid complex consists of small muscles, we planned small doses with the goal of minimizing adverse effects and vocal trauma. Our first approach was to inject 2.5 U into one vocal cord. This injection had little effect. We then gave an additional 7.5 U, which caused a vocal cord paresis and a period of breathy dysphonia but 90% improvement of vocal function. In keeping with our goal of minimizing the total exposure to BOTOX, we decided to explore bilateral, low-dose injections. This decision also paralleled our theory that weakening or paralyzing one vocal cord stresses the remaining vocal cord and exaggerates the dystonic symptoms. We therefore initiated a first-treatment program of injecting both vocalis muscles with 3.75 U. All patients experienced benefit. Initially there was an effect within the first 24 hours, followed by a hypophonia that was maximum at the third post-injection day. This breathy speech typically lasted 4 to 14 days and was mild, but lasted 57 days in one patient. Some patients also experienced a mild choking sensation when drinking fluids, although there were no cases of aspiration. Patients found that drinking slowly compensated adequately for this symptom until it resolved. Patients' speaking improved from 60% to 100% of normal function with a mean of 90%, and the duration of effect was from 3 to 4 months. Patients often requested reinjection before returning to their pretreatment level of functioning. When we performed 2-week follow-up laryngeal EMG, occasional evidence of denervation could be found.

Owing to the prolonged period of breathy hypophonia in some of the patients receiving 3.75 U per vocal cord, we modified our first treatment protocol by reducing the dose to 2.5 U per vocal cord. Although there was a trend for decreased duration of breathiness, choking, and duration of benefit at 2.5 U, the differences were not statistically significant. Two patients, however, failed to have any noticeable effect at the lower dose and had to be reinjected. Because of the lack of significant difference in the duration or degree of benefit of these two doses, our current protocol is to initially inject 2.5 U per cord except when the patient finds it impossible to make a return visit in 2 weeks should the injection have no effect. In these patients a dose of 3.75 U per cord is given. For repeat injections, we initially injected either 3.75 or 2.5 U per cord. We have begun to give some patients 2.5 U unilaterally or 1.25 U bilaterally on follow-up to minimize the length of hypophonia, since there often appears to be some residual weakness at the time of the follow-up injection.

The adverse effects from laryngeal BOTOX injections included a mild breathy dysphonia for a short period of time in 45% of patients and mild choking on fluids for the first several days in 22%. Several patients hyperventilated and became dizzy trying to speak while hypophonic. Several patients coughed up blood-tinged sputum and/or had a sore throat. One patient had itching but no rash.

Nerve Section. Of the adductor vocal group, nine were patients who had failed a recurrent laryngeal nerve section. This group, previously reported,[20] included four men and five women ranging in age from 36 to 62 with a mean of 50. They all failed RLN section from 0 to 4 years postoperatively (mean, 1.8 years). Four of the patients had more than one procedure performed on the nerve or vocal cord to try to turn failure into success. Laryngeal EMG was performed on all patients; most showed signs of chronic denervation with few and very small potentials and occasional fibrillation potentials. We injected most of the patients with 2.5 U unilaterally. This was given in the functional cord in most patients with an improvement of 0% to 100% with a mean of 81% as compared to 10% to 80% with a mean of 59% when the paralyzed cord was injected.

Anterior Commissure Release. In addition to the nerve section failures we have treated three patients who failed an anterior commissure release procedure. In these patients the larynx appeared foreshortened, but the adductor spasms were as intense as in the nonoperated group. These patients were also given 2.5 U per vocal cord, and all experienced benefit. The spasms remitted, but because of the laxity of the vocal cord from the release, most noticed a narrowed pitch range. The duration of the breathy hypophonia also was extended in this group.

Abductor Laryngeal Dystonia. With our growing experience, we cautiously elected to treat abductor laryngeal dystonia with injection of BOTOX into the PCA muscle. We informed the patients that excessive weakening of the PCA muscle might cause airway distress and might necessitate a temporary tracheostomy. Doses of 1.25 to 5 U were given in one to four treatments to weaken one or both PCA muscles in 12 patients. Marked improvement was seen in 8, with a mean improvement to 57% and a return of mean maximal functional performance to 80% of normal. Follow-up treatments required smaller toxin doses. The adverse effects included brief choking on fluids without aspiration and mild stridor on exertion in 2 patients. There were no significant breathing difficulties, even in the cases in which both PCA muscles were injected.

Adductor Laryngeal Breathing Dystonia. In addition to the patients who had phonatory symptoms due to laryngeal dystonia, we identified three patients who had paradoxical motion of the vocal cords during respiration. These patients were not hypoxic, but produced moderate to severe inspiratory stridor. This symptom disappeared as soon as the patients went to sleep, and took a short while after awakening in the morning to reappear. After a thorough otolaryngologic, neurologic, and pulmonary workup, we treated two of these patients with BOTOX with decrease or cessation of the symptoms. A complete description of these patients and their test results will be published separately.

DISCUSSION

The data from our previous publications,[1,9,15,19-21,23] our current series, and reports of other authors support the conclusion that "spastic dysphonia" and "whispering dysphonia" are focal laryngeal forms of dystonia. Our data on age of onset, sex preponderance, Jewish/non-Jewish ratio, family history, and involvement of other body parts are consistent with those of other authors and with those of our total dystonia group.

The average age at onset in our entire group was 38 for both the adductor and abductor forms. The average age of patients who had primary dystonia of the larynx and another body part was 31, since patients with early-onset disease are more likely to have more than one site involved.

Of the 260 patients who had the larynx as their primary site of onset, 27 (10.4%) had spread to another body part. These data suggest that patients should be advised of possible spread and be followed and reexamined on a regular basis for signs of other dystonic involvement. The family history was also significant, with 44 of 260 patients (17%) with primary laryngeal dystonia having a family history of dystonia. Family studies of childhood onset idiopathic dystonia show an autosomal dominant inheritance with reduced penetrance. A gene locus marker located on the 9q chromosome has just recently been established by our group and others, and this finding opens new doorways for the understanding and possible treatment of the disorder.[24] Therefore, it is of paramount importance to obtain a family history and have genetic counseling provided where necessary.

Recurrent laryngeal nerve section originally seemed to be the treatment of choice for SD. However, many late failures were found leaving a poor voice with a continued paralyzed vocal cord. We believe that the return of symptoms in these patients is due to stressing the remaining functioning vocal cord, thereby intensifying the dystonic symptoms.

Ludlow et al[25] and Miller et al[26] have injected higher doses of toxin (up to 60 U over three visits) into one vocalis muscle in patients with SD. Since the goal of this treatment method is unilateral vocal cord paralysis, we see little advantage of this technique over recurrent laryngeal nerve section. We have theorized that surgical therapy may ultimately fail because the contralateral functioning vocal cord hyperadducts. This hyperadduction stresses the remaining functional vocal cord and exaggerates the underlying dystonic state, causing additional dysfunction and a return of the dysphonia.

Our experience with 210 patients has shown that local injections of BOTOX into laryngeal muscles is a relatively safe and effective mode of therapy for laryngeal dystonia. In contrast to surgical therapy, BOTOX injections have the advantage of being given on an ambulatory basis; both vocal cords can be treated; and the toxin is given under EMG control for precise localization of the most active part of the muscle complex. Graded weakening can be achieved by using low dosages and repeating the injections to achieve the optimum weakness desired. If too much weakness is produced, the strength gradually returns with time. The procedure is very acceptable to patients with very satisfactory vocal results. It is too soon to tell whether patients will become refractory to this form of therapy. To date we have not found anyone who has become refractory with laryngeal injections or sustained a disability from laryngeal toxin injections.

CONCLUSION

Laryngeal dystonia is a disorder of central motor processing that can cause adductor spasms ("spastic dysphonia"), abductor spasms ("whispering dysphonia"), and adductor breathing dystonia. Laryngeal BOTOX injections are performed percutaneously, on an ambulatory basis under EMG control. Graded weakening can be achieved by using small dosages and injecting additional toxin as needed. If too much weakness is produced, the strength gradually returns with time. Our data suggest that BOTOX injection is the treatment of choice for dystonic symptoms of the larynx.

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MANAGEMENT OF SUBGLOTTIC STENOSIS IN THE ADULT

THOMAS V. MCCAFFREY, MD, PHD
ROCHESTER, MINNESOTA

Twenty-one adult patients were surgically treated for severe subglottic stenosis refractory to endoscopic treatment. Patients were treated by anterior or anterior and posterior cricoid division with costal cartilage grafting. Seventy-six percent of the patients were successfully decannulated. Success of treatment was not dependent on cause of the stenosis or age or sex of the patient. There was a significantly better outcome ($p < .05$) in patients with isolated subglottic stenosis versus those with combined glottic and subglottic stenosis.

KEY WORDS — cartilage graft, laryngeal stenosis, subglottic stenosis, surgery, Wegener's granulomatosis.

Management of stenosis of the subglottic larynx remains one of the most challenging problems facing the laryngologist. The basic principle for repair of subglottic stenosis, providing substantial circular architecture over which respiratory epithelium may regenerate, was clearly stated by Conley[1] in 1953. But practical and reliable methods for achieving this goal have been remarkably evasive. Some of the endoscopic treatment methods used have been endoscopic dilation, intralesional steroid injection, carbon dioxide (CO2) laser excision, or mucosal flaps.[2-4] Each of these endoscopic methods has been successful in some cases; however, severe subglottic stenosis must usually be treated by open surgical techniques to restore adequate cartilaginous or bony support for the airway. Two methods of surgical treatment of severe subglottic stenosis have been widely used: segmental resection of the stenosed segment, and expansion of the stenosed segment with bone or cartilage grafts. Although segmental resection of tracheal stenosis below the cricoid is widely used, segmental resection of the subglottic cricoid involves substantial risk to vocal cord function through injury either to the recurrent laryngeal nerves or to the cricoarytenoid joints. For this reason, most surgical approaches for repair of subglottic stenosis have employed some type of cricoid expansion with grafting. Looper,[5] in 1938, was the first to describe the use of hyoid bone for grafting the subglottis. Since that time, several other authors have reported favorable results in using the hyoid bone as a free graft or as a pedicled flap based on the sternohyoid muscle for reconstruction of the subglottis.[6-10] Hyoid bone grafting is useful for expanding the anterior glottis but may not be adequate for posterior subglottic or circumferential subglottic stenosis. In 1956, Rethi[11] described a technique for repair of subglottic stenosis that included both anterior and posterior vertical division of the cricoid and stenting. This technique with the addition of anterior or both anterior and posterior cartilage grafting has been effectively used by Cotton[12] and Cotton and Myer[13] to treat severe subglottic stenosis in pediatric patients. This report describes our results using these techniques for treating severe subglottic stenosis in adults.

PATIENTS

The patients reviewed in this study were adults with subglottic stenosis refractory to repeated endoscopic attempts at dilating or resecting the stenosis with the CO2 laser. All patients had a previously placed tracheotomy or had severe limitation of activity due to airway insufficiency. The average patient age was 50 years of age with a range of 15 years to 78 years. The cause of the stenosis was trauma in six patients, intubation injury in three, Wegener's granulomatosis in seven, neoplasm in one, cicatricial pemphigoid in one, and idiopathic in three.

METHODS

The surgical technique was consistent in all patients except for slight modifications depending on the vertical extent of the stenotic segment.

If a tracheotomy is not present, a tracheotomy is initially performed below the site of the stenosis. The tracheotomy is performed either under local anesthesia or under general anesthesia after bronchoscopic intubation.

A horizontal neck incision is made 2 to 3 cm above the tracheotomy site and the strap muscles over the larynx are retracted laterally. The thyroid isthmus is divided. A midline vertical cut is made in the anterior cricoid arch with a saw or knife and extended inferiorly into the trachea and superiorly into the thyroid cartilage beyond the superior and inferior extent of the stenosis (Fig 1A,B). The incision is made through the anterior commissure if there is glottic stenosis in addition to subglottic stenosis. Retraction of the cricoid ring then shows the extent of the stenosis. In most cases the rigidity of the cricoid cartilage in adults requires a posterior division of

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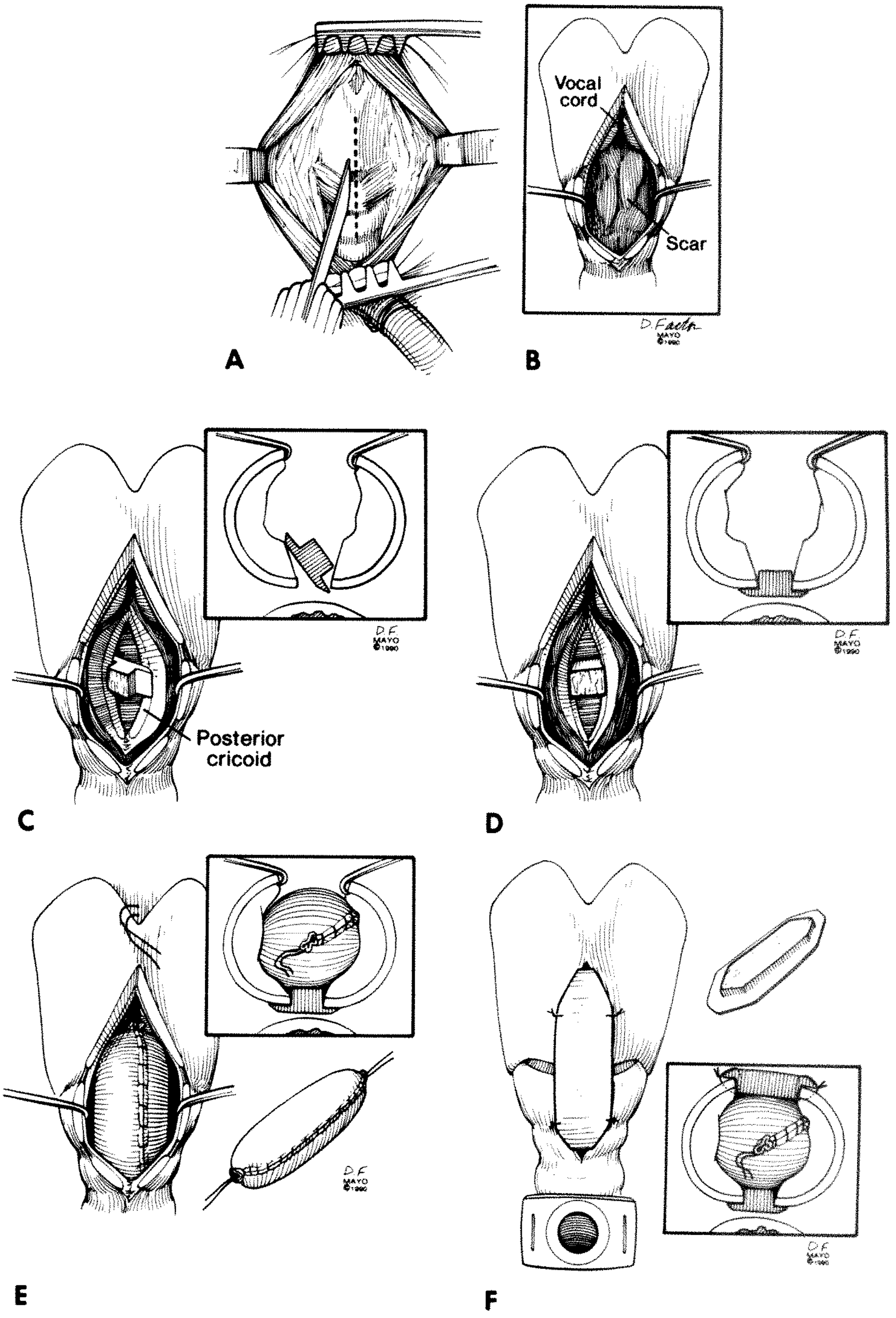

Fig 1. Techniques. A) Retraction of strap muscles and exposure of anterior larynx and trachea. B) Retraction of divided anterior cricoid ring and exposure of stenotic segment. C) Placement of posterior cartilage graft after division of posterior lamina of cricoid cartilage. Inset) Axial view of insertion of posterior cartilage graft. D) Posterior cartilage graft in place. No fibrosis or mucosa is excised. Inset) Axial view of placement of posterior cartilage graft. E) Placement of finger cot stent covered with split-thickness skin graft. Inset) Axial view of stent placement. F) Placement of cartilage graft in anterior defect of subglottis. Graft is secured with monofilament suture. Inset) Axial view of anterior graft placement.

the cartilage to permit expansion of the airway. The posterior body of the cricoid is divided in the midline with a knife or saw. When this is done a substantial expansion of the airway can be achieved with minimal retraction. No attempt is made to excise mucosa or scar within the lumen of the airway.

Cartilage for grafting is obtained from the fifth or sixth costal cartilage. An incision is made over the costal cartilage, and the cartilage with its anterior perichondrium attached is removed by means of rib elevators. The cartilage is fashioned into anterior and posterior grafts. The posterior graft is a T-shaped graft with flanges to fit under the body of the cricoid cartilage. The anterior graft is a fusiform graft with an overriding expansion to prevent inward displacement. In both cartilage grafts the surface-bearing perichondrium faces toward the lumen of the larynx.

After the posterior perichondrium of the body of the cricoid is elevated approximately 2 mm on each side, the posterior graft is wedged into the posterior split (Fig 1C). Its flange prevents displacement and no additional fixation is required. Usually 2 to 3 mm of posterior expansion is achieved. However,

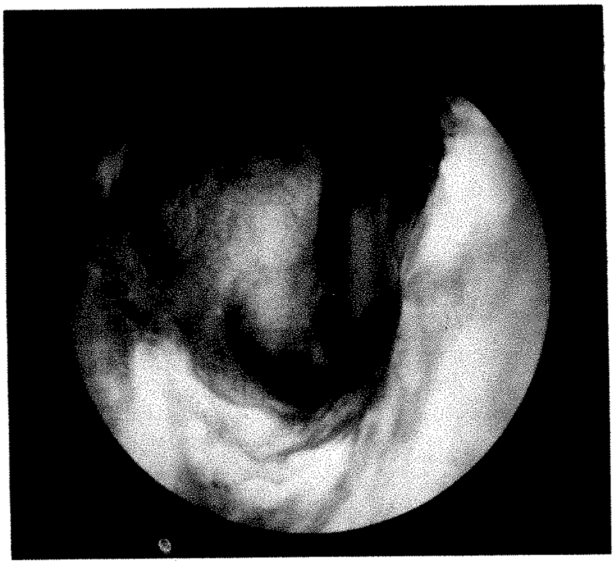

Fig 2. Right-angle telescopic view of subglottis 1 month following reconstruction. Diameter is normal, and pale areas on anterior and posterior walls are healed skin grafts.

because of the rotation of the cricoid fragments that are still attached to posterior perichondrium, there is an 8- to 12-mm expansion produced anteriorly (Fig 1D).

An intraluminal stent is inserted. The stent consists of a 0.3-mm-thick split-thickness skin graft tied over a soft sponge within a finger cot. The stent is fixed above and below with sutures (Fig 1E). The anterior cartilage graft is shaped to fit the anterior defect and sutured in place with monofilament suture (Fig 1F).

The intraluminal stent is endoscopically removed after 3 to 4 weeks. The tracheotomy is removed when the airway is stable and considered adequate (Fig 2).

RESULTS

Twenty-one patients personally treated by the author for subglottic or combined glottic and subglottic laryngeal stenosis are included in this report. There were 8 males and 13 females treated. The patients' ages ranged from 15 to 78 years.

The cause and site of the laryngeal stenosis varied, but in all cases endoscopic management of the stenosis by dilation, CO_2 or neodymium:yttrium-aluminum-garnet laser excision, or a combination of endoscopic treatment methods had failed to relieve the stenosis (see Table).

Prior to surgical treatment all patients had either a tracheotomy tube in place or significant restriction of normal daily activities resulting from airway insufficiency. The diameter of the stricture site was less than 4 mm in all cases as measured by a rigid 4-mm–outside diameter bronchoscope at the time of the repair.

One patient had obstruction resulting from neoplasm (chondroma of the cricoid cartilage), three from endotracheal tube injury caused by prolonged or traumatic intubation, six from external blunt trauma, and seven from Wegener's granulomatosis that was definitely diagnosed histologically in four and strongly suspected but not histologically confirmed in three. In all cases of Wegener's granulomatosis the inflammatory process was either quiescent or medically controlled at the time of operation. One patient had cicatricial pemphigoid of the larynx and nasal airway, and three patients had no

PATIENT DATA

Age	*Sex*	*Site of Stenosis*	*Cause of Stenosis*	*Prior Tracheotomy*	*Procedure*	*Airway*
65	M	Subglottic	Chondroma	No	A, CCG, STSG	Good
51	M	Glottic-subglottic	Endotracheal tube	Yes	AP, CCG, STSG	Tracheotomy
42	F	Glottic-subglottic	Endotracheal tube	Yes	AP, CCG, STSG	Good
63	F	Subglottic	Endotracheal tube	No	A, CCG	Good
42	M	Glottic-subglottic	Trauma	Yes	A, hyoid, mucosa	Tracheotomy
15	M	Subglottic	Trauma	Yes	AP, CCG, STSG	Good
65	F	Subglottic	Trauma	No	A, hyoid, STSG	Good
78	F	Subglottic	Trauma	Yes	A, CCG, STSG	Good
15	M	Subglottic	Trauma	Yes	AP, CCG, STSG	Good
60	F	Glottic-subglottic	Trauma	Yes	AP, CCG, STSG	Tracheotomy
74	F	Subglottic	Wegener's granulomatosis	Yes	AP, CCG, STSG	Good
61	F	Subglottic	Wegener's granulomatosis	Yes	AP, CCG, STSG	Good
29	F	Subglottic	Wegener's granulomatosis	Yes	AP, CCG, STSG	Good
42	M	Subglottic	Wegener's granulomatosis	Yes	AP, CCG, STSG	Good
74	M	Subglottic	? Wegener's granulomatosis	Yes	AP, CCG, STSG	Good
24	F	Subglottic	? Wegener's granulomatosis	Yes	AP, CCG, STSG	Tracheotomy
41	F	Subglottic	? Wegener's granulomatosis	No	AP, CCG, STSG	Good
64	M	Glottic-subglottic	Pemphigoid	Yes	AP, STSG	Good
52	F	Subglottic	Idiopathic	Yes	AP, CCG, STSG	Good
56	F	Subglottic	Idiopathic	Yes	AP, CCG, STSG	Good
44	F	Subglottic	Idiopathic	No	A, CCG	Tracheotomy

A — anterior cricoid only divided, AP — anterior and posterior cricoid divided, CCG — costal cartilage graft, STSG — split-thickness skin graft and stent.

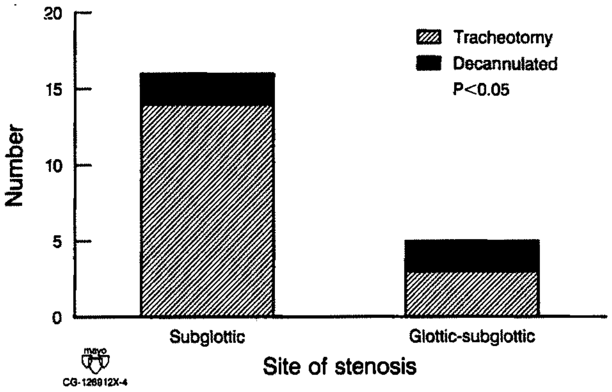

Fig 3. Success and failure rates for correction of isolated subglottic stenosis and combined glottic and subglottic stenosis. Difference between decannulation rate of subglottic stenosis versus combined glottic and subglottic stenosis is statistically significant ($p < .05$ by χ^2 statistic).

specific diagnosis.

Nineteen patients were treated by the costal cartilage grafting technique as described and two patients were treated with a pedicled hyoid bone graft.

Overall, 16 of the 21 patients (76%) obtained a satisfactory airway. That is, they were able to be decannulated and were able to function in normal daily activities without restriction. The mean time between operation and decannulation in this group was 8.5 weeks with a range of 4 to 20 weeks. In six of these cases formation of granulation tissue in the reconstructed subglottis resulted in a delay of decannulation. Removal of the granulation tissue required from one to three CO2 laser excisions. Five patients (24%) have not been decannulated and continue to require a tracheotomy tube.

Failure to correct the stenosis is not dependent upon the cause of the stenosis ($p > .1$ by the χ^2 statistic), and there was no detectable effect of age or sex on success rate. The preoperative diameter of the stenosis or the preoperative need for the tracheotomy does not influence the outcome of the procedure. However, there is a significant effect of site and length of the stenosis on the success rate of the procedure. Three of 5 patients with long stenotic segments producing both glottic and subglottic stenosis failed decannulation, while only 2 of 16 patients with isolated subglottic stenosis failed decannulation (Fig 3) ($p < .05$ by the X^2 statistic).

No patients experienced dysphagia or aspiration as a result of the procedure, although some patients did have mild breathiness following the procedure that improved with time.

DISCUSSION

Although many methods for repairing subglottic stenosis have been reported, the common principle remains the establishment of a structurally stable circumferential airway. When the integrity of the cricoid cartilage is not affected, as in weblike stenosis of limited thickness, simple dilation or CO2 laser excision is an effective treatment and a high success rate can be expected. However, in those thick stenoses in which there is compromise of the cricoid cartilage either by collapse or by scarring that extends to involve cartilage, simple endoscopic excision is not effective in establishing an airway. Use of the CO2 laser to resect thick scarring in the subglottis results in exposure of cartilage. This leads to delayed reepithelialization and further fibrosis, with recurrence of the stenosis. Patients treated in this way will have immediate improvement in their airway but experience gradual restenosis over a period of 2 to 6 weeks. Often the recurrent stenosis is more severe than the initial problem.

The principles advocated by Rethi[11] for the correction of severe subglottic stenosis can well be applied to the modern treatment of this problem. Rethi recognized that to produce wide expansion of the subglottis both the anterior ring and posterior body of the cricoid cartilage must be divided. Only in this way can sufficient expansion be produced. In addition, Rethi advocated minimal resection of scar. Resection of scar in the subglottis encourages further stenosis by the exposure of cartilage, and contraction is enhanced by the absence of epithelium.[11] Cotton and Myer[13] have validated these observations in the treatment of severe subglottic stenosis in children.

The extensive work of Cotton et al[12,13] on pediatric laryngeal stenosis has contributed the use of costal cartilage grafting of the anterior and posterior defects produced in the cricoid cartilage. This establishes a stable ring structure to support the subglottic airway.

Skin or mucosal grafts have been widely used in the past to reepithelialize the oral cavity, pharynx, and larynx. The advantage of their use in the reconstruction of the subglottic airway is to provide rapid epithelialization in order to prevent scar contracture and granulation. Although exposed cartilage in the airway will not accept a skin graft, the graft does adhere to the exposed vascularized tissue and appears to enhance the healing process and speed complete epithelialization. Since the skin graft produces a squamous nonciliated epithelium, there is a tendency to develop some crusting due to mucus accumulation at the graft site. This may be noticed as a tendency to cough out dry flakes of mucus occasionally, but has not been a significant problem.

The techniques used in this series appear to be effective in correcting severe subglottic stenosis resulting from a wide variety of causes including external trauma, endotracheal tube injury, inflammatory conditions including Wegener's granulomatosis, pemphigoid, and idiopathic scarring. Cause of stenosis, age, and sex have no detectable effect on success rate of correction of the stenosis, with approximately 75% of patients able to be decannulated.

The site of stenosis has a significant effect on outcome. In this series only 40% of patients with combined glottic and subglottic stenosis were able to be decannulated; however, 88% of those with isolated subglottic stenosis were decannulated. The factor that prevents decannulation in the majority of the combined stenoses is fixation of the vocal folds and an inadequate airway at the glottic level, rather than failure to correct the subglottic stenosis. Although arytenoidectomy was not used in this series to treat stenosis at the glottic level, it may prove to be a useful technique when combined with subglottic expansion for treating laryngeal stenosis involving the glottis and subglottis. Further study will no doubt provide better solutions to this most challenging problem.

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SURGICAL TREATMENT OF LARYNGEAL WEB WITH MUCOSA GRAFT

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Surgical treatment of laryngeal webbing varies with the extent and site of the web. An extensive one seems to be best treated by laryngofissure and skin or mucosa transplantation. Recent experiences with four cases of thick glottal webbing indicated that a mucosa graft was better for the voice result than a skin graft. For success in the airway and voice results, the salient points in surgery include 1) precise midline thyrotomy, 2) shaping of the vocal cord under fiberoptic control, and 3) mucosa grafting with the combined use of a pliable stent or fibrin glue for fixation.

KEY WORDS — laryngeal web, mucosa graft.

Treatment for a laryngeal web or stenosis varies with its location and extent, and a wide range of procedures are now available for this purpose. The surgical treatment most commonly used for a thin laryngeal web would probably be endolaryngeal division of the web with a knife[1-9] or carbon dioxide (CO2) laser,[10-19] followed by temporary placement of a keel to prevent readhesion. More secure keel placement can be achieved by the laryngofissure technique as reported by McNaught,[20] Montgomery,[21-23] and others.[24-29] However, a thick glottic stenosis extending from the glottis to the subglottis usually requires a mucosal flap, skin, or mucous membrane graft to cover the wide raw surfaces, as strongly advocated by Montgomery.

Recently, we have treated four cases of laryngeal webbing or severe stenosis. In the first case, three types of procedures were performed one after another, each in an attempt to make a further improvement in the voice. They were 1) endolaryngeal section of the web and keel placement, 2) skin grafting, and 3) replacement of the skin graft by a mucous membrane graft. Since the voice quality obtained by mucosa grafting was much superior to that obtained by the other two methods, the last two cases of complete glottal stenosis and one congenital glottosubglottal web were all treated with a mucosa graft. The results were all satisfactory both in airway and voice.

SURGICAL PROCEDURES

Under general anesthesia administered through tracheostomal intubation, laryngofissure is performed with particular care to cut the thyroid cartilage precisely at the midline. After the midline section of the thyroid cartilage alone, a hypodermic injection needle is inserted between the incised edges of the thyroid cartilage into the laryngeal lumen to see by a pernasal flexible fiberscope whether it hits the anterior commissure precisely.

Under fiberscopic control, the web is cut little by little in the ventrodorsal direction. Judgment on whether or not to further trim the incised edges of the web off to a quasi-normal glottal shape should be made on the basis of fiberscopic findings in the glottis as seen from above, not as seen from the front through the laryngofissure. After excision of the web or stenosis, the areas void of mucosa are roughly measured and a mucosa graft sufficient in size is taken from a deep portion of the lower lip to cover the bilateral mucosa defects at the glottis (Fig 1A). The graft, deprived of fat tissue, is cut in half to match the defect.

The graft is then sutured in place to the wound with absorbable sutures (Dexon 6-0) when the laryngofissure is primarily closed (case 4). When the fissure must remain open for a while for stent placement, nylon sutures (6-0) may be used instead. In the latter case, the incised skin edges are pulled inward and sutured with the anterior portion of the graft, covering the incised edge of the thyroid cartilage. Fixation of the graft is accomplished by either stent placement (Fig 1B) or application of fibrin glue (Fig 1C).

A special stent was devised for the purpose of fitting to any complicated configuration with adequate pressure. A soft silicone (ear putty) that contains a hard silicone as a core is wrapped in a finger portion of a surgical glove. This pliable soft silicone is put in place so as to compress the graft gently and is fixed by mattress sutures that pass the bilateral cervical skin and the hard silicone core for stabilization of the stent in place (Fig 1D).

Some 10 days after grafting, the stent is removed, and the laryngofissure is usually kept open for an-

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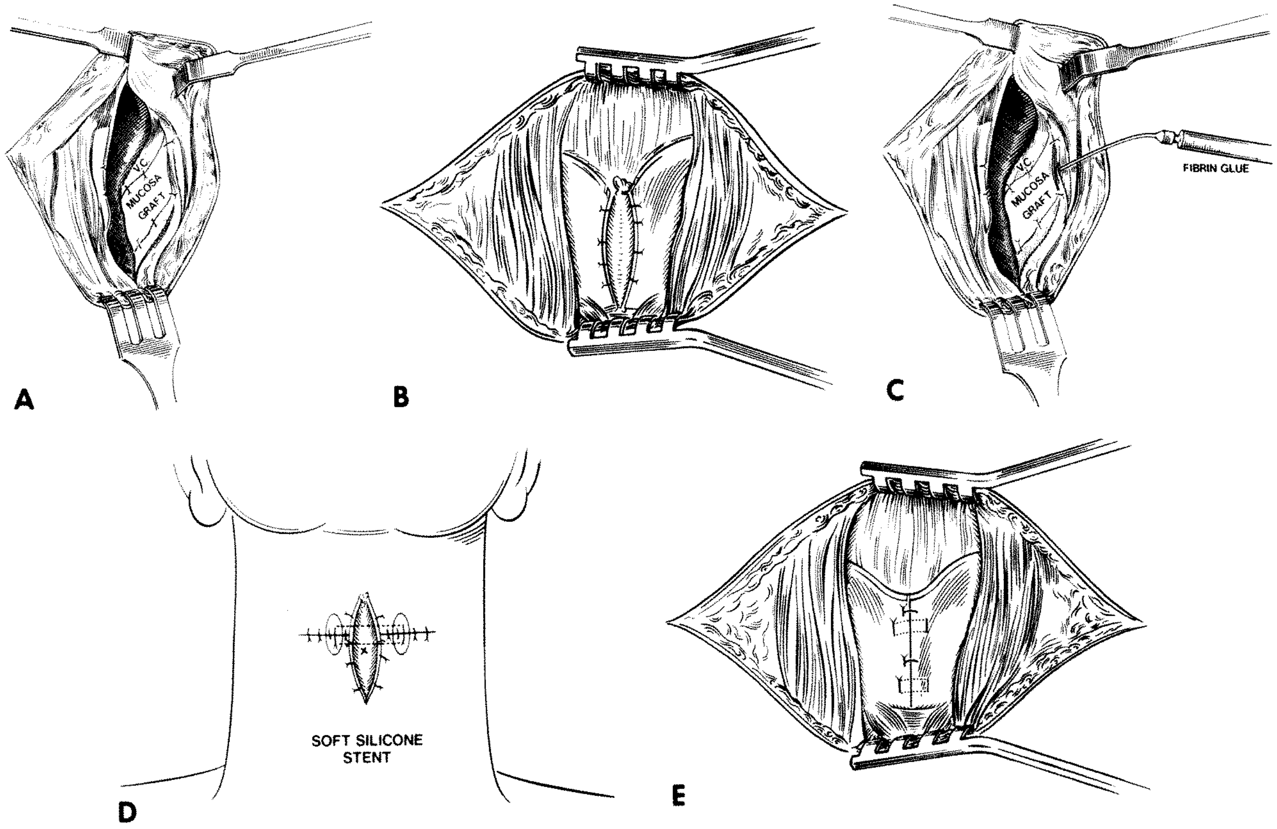

Fig 1. Techniques. A) Raw surface created by division of laryngeal web is covered with mucosa graft taken from mucous membrane of lower lip. VC — vocal cord. B) For compression of mucosa graft, pliable silicone stent that consists of surgical rubber glove, soft silicone, and hard silicone as core is placed at glottis. C) Mucosa graft, after being sutured to wound of vocal cord (VC), is further fixed by fibrin glue, dispensing with use of stent. D) Pliable silicone stent is fixed in place with mattress suture. E) Laryngofissure is primarily or secondarily closed, depending on whether there is dyspnea or not before operation. Without preoperative dyspnea, it is primarily closed, as illustrated, after mucosa grafting with fibrin glue.

other week to ensure complete epithelialization at the edges. Before closure of the laryngofissure and tracheostoma, the anterior laryngeal slit and the stoma are manually closed in order to confirm that an adequate airway and vocal function are restored. Airway resistance at the glottis during respiration and phonation can be measured at this time by temporary manual closure of the laryngofissure: the airway resistance at the glottis is equal to the subglottal pressure as measured via the tracheostoma divided by the oronasal airflow rate.

If there was no airway obstruction before operation, as in case 4, the laryngofissure can be closed primarily at the time of web excision and mucosa grafting (Fig 1E). The grafted mucosa is then fixed to the wound by fibrin glue, and obstructive stent placement can be dispensed with. It is important to inject fibrin glue under the graft after the graft is precisely placed and fixed by about six 6-0 absorbable sutures (Fig 1C). Redundant glue may be squeezed out by gently pressing the graft.

CASE REPORTS

CASE 1

A 26-year-old woman had developed an adhesion following repeated excisions of laryngeal papillomas since infancy. She had had a tracheostomy elsewhere before visiting us.

Under general anesthesia, laryngomicrosurgical section of the web was performed and a silicone keel was placed to remain for 2 months. Readhesion did not occur but the voice remained almost as breathy as before (Fig 2A). A second operation consisting of laryngofissure and skin grafting was performed, again with rather disappointing results in voice (Fig 2B) and expectoration, as followed up for over 1 year. Next, again via laryngofissure, the grafted skin was replaced with a mucosa graft that was taken from the deep portion of the lower lip. The mucosa was sutured to the raw surface of the vocal cords and compressed for 10 days by the special pliable stent mentioned above. At 42 days after removal of the stent, when the epithelialization of the anterior commissure region had been completed, the laryngofissure was closed. Later, thyroplasty type I was added to improve the glottal closure during phonation. The vocal improvement after mucosa transplantation was remarkable and has been maintained 4 years postoperatively (Fig 2C).

CASE 2

An 11-year-old boy gradually developed a subtotal adhesion of the vocal cords after laryngeal trau-

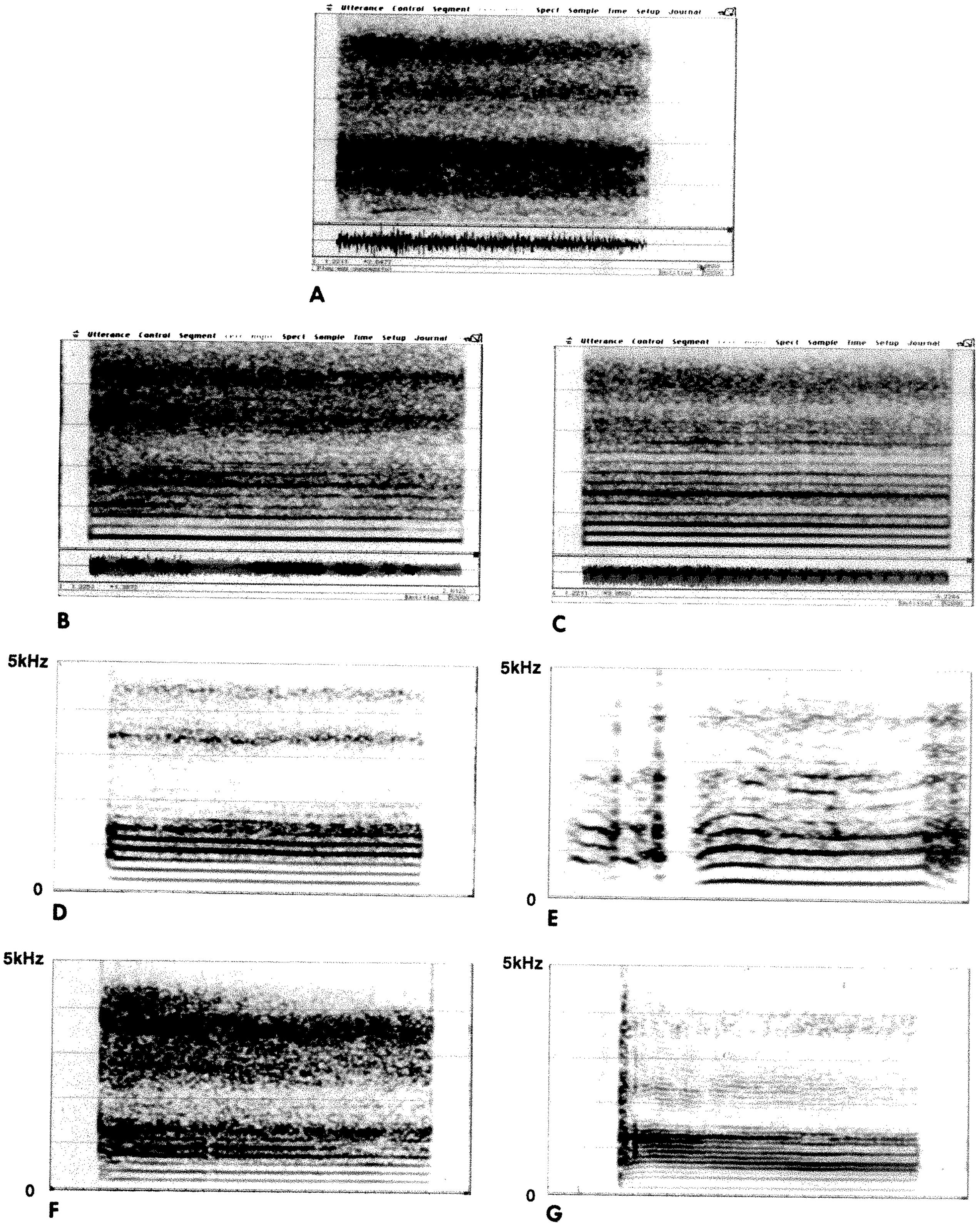

Fig 2. Sonagrams. A-C) (Case 1) A) Sonagram (narrowband) taken before skin grafting showing severely breathy voice containing no harmonics. B) Sonagram taken after skin grafting. Voice is improved after operation, but still fairly breathy, featuring mixture of harmonics and noise. C) Sonagram after replacement with mucosa. Harmonic components are dominant over noise. D) (Case 2) Sonagram taken after operation. Patient was aphonic before operation. Voice after operation was fairly good, as demonstrated by dominant harmonic components on sonagram. E) (Case 3) Sonagram taken after operation. Patient was aphonic owing to complete obstruction of glottis before operation. Her voice was still fairly hoarse after operation. She had vocal and articulatory problem resulting from central nerve discoordination. F,G) (Case 4) F) Sonagram taken before operation. Severe breathiness of voice is shown by dominant noise on sonagram. G) Sonagram taken after operation. Voice improved substantially after operation, as demonstrated by dominant harmonic component on sonagram.

ma he sustained while he was playing on a jungle gym. Gradually increasing dyspnea necessitated tracheostoma.

This patient was treated with mucosa transplantation to the raw surface of both vocal cords and the interarytenoid region (posterior commissure). Basically, the technique used for mucosa grafting in this patient is the same as the third operation in the first case, including laryngofissure, mucosa graft, placement of a pliable silicone stent, and later closure of the laryngofissure followed by closure of the tracheostoma. Since the operation he has had no dyspnea in daily life and the voice was restored to nearly normal although slightly rough (Fig 2D).

CASE 3

A 39-year-old woman had suffered a severe head injury in a traffic accident that necessitated prolonged intubation. Subsequent severe tracheolaryngeal stenosis was partially treated elsewhere by end-to-end anastomosis of the trachea, and then she was sent to us for treatment of complete laryngeal obstruction. The treatment employed was essentially the same as in the previous two cases, except that the scar was more widely spread and required not only the mucosa graft but a false vocal cord flap as well for coverage of the defect. Fibrin glue was used in this patient. The stoma was closed, and normal respiration and acceptable voicing, although slightly rough and discoordinated, became possible (Fig 2E). She is now under speech therapy for dysarthria that resulted from brain damage.

CASE 4

A 21-year-old man had had a breathy voice due to a congenital laryngeal web that extended over the membranous portion of the vocal cord (Fig 2F). He had not complained of dyspnea, except during hard exercise. The surgical steps performed include tracheostomy, intubation anesthesia, laryngofissure, mucosa transplantation, and closure of the fissure. In contrast to the previous cases, a mucosa graft was adhered to the vocal cord wound with fibrin glue and no stent was placed; hence, primary closure of the laryngofissure was possible. The mucosa graft needed to be placed far anterior over the incised thyroid cartilage edges to suture with the skin edge so as to prevent anterior readhesion. The tracheostoma was closed about 1 month after laryngofissure. The voice has been much improved, as shown by the sonagram in Fig 2G, and he said he became much less fatigued during daily conversation.

To sum up the results in the four cases, the airway problem has been solved to the extent that no tracheostomy is necessary in any of them. However, in case 3, in which the vocal cord movement is apparently restricted on respiration by a rather narrow glottis, slight dyspnea was present on hard exercise. Voice improvements were generally satisfactory, as shown by the sonagrams in Fig 2. The patient with brain damage (case 3) has had an articulation problem requiring rehabilitation.

DISCUSSION

REVIEW OF SURGICAL PROCEDURES FOR LARYNGEAL WEBBING

A wide range of surgical procedures are now available for treating laryngeal webbing or stenosis. Basically, selection of the method to be employed for a specific case is made on the basis of the site and extent of the lesion. If it is thin or limited to the anterior part of the glottis, the treatment of choice has been endolaryngeal division of the web followed by placement of a keel.[1-9]

Recently, the success rate of the endolaryngeal method seems to have been further raised by the use of the CO_2 laser.[10-16] New, sophisticated techniques for creating a mucosal flap endoscopically with the CO_2 laser have also been developed, with improvement in the results; one is the microtrapdoor flap[17,18] and the other is a spot-welded technique.[19]

Langman et al,[8] however, experienced failure with the microtrapdoor flap in three cases and were motivated to develop an endolaryngeal technique of placing a keel for posterior stenosis. The limitations of the CO_2 laser technique have been pointed out by many surgeons. As features indicating a poor prognosis after a CO_2 laser procedure, Simpson et al[14] listed a thick circumferential web and posterior stenosis, recommending laryngofissure as the best approach to such severe stenosis. The laryngofissure technique remains a relatively safe and reliable method for complicated, complete, or posterior laryngeal webbing, as suggested by Benjamin[24] and McIlwain.[25] In the laryngofissure approach, after web excision the anterior commissure is usually kept open and separated by a McNaught[20]-type keel left for some time to secure epithelialization there. Montgomery[21-23] developed a variety of external laryngeal techniques, still most reliable even in difficult cases, with the use of mucosal pedicled flaps, skin or mucous membrane grafts, and new types of stents. Various modifications followed especially for difficult cases.[26-29]

Success or failure in laryngeal web surgery should be judged on the criteria of 1) an adequate airway without a tracheostomy and 2) voice. The key issues in the surgery always involve how to prevent readhesion and scar formation, which will without doubt hinder the vocal cord vibration. The CO_2 laser, although quite a useful tool, would not be able to remove a thick web without creating a scar, however minimal it might be. For a thick web, covering of the wide raw surfaces with a mucosal flap, skin, or a mucosa graft still seems preferable.

MUCOSA TRANSPLANTATION

Our experience with the first case of laryngeal webbing (case 1), in which the skin transplant was later replaced with a mucosa transplant, clearly demonstrated that the latter is much superior to the former in terms of quality of voice after operation. Martin et al[30] used a fibrin glue endoscopically for coverage of the vocal cord wound. Okamura et al[31] demonstrated experimentally that mucosa grafting for the raw surface of the vocal cord was of critical importance for normal vibration of the vocal cord, and recommended also the use of tissue adhesive in endolaryngeal fixation of the graft without suturing. As to reconstruction after hemilaryngectomy, Hirano et al[32] reported that the vocal function was good more frequently with the use of a mucosa transplant than with a skin flap, although the mucosa graft posed a problem of occasional necrosis. Kojima et al[33] and Omori et al[34] applied a mucosa graft to an anterior laryngeal web that had followed a partial laryngectomy, via laryngofissure, using a human fibrin glue and dispensing with a stent. Previous reports in the literature pertaining to laryngeal webs do not say much about the voice quality after treatment. Our present experience together with an analysis of preoperative and postoperative voice supports the use of a mucosa transplant for covering the raw surface after excision of a web.

PROBLEMS IN MUCOSA TRANSPLANTATION FOR LARYNGEAL WEBBING

Precise Midline Thyrotomy. Accurate midline division of the laryngeal web is a prerequisite to success in its treatment. A common technique to secure precise midline cutting at the anterior commissure is the use of a Kelly clamp as a guide, introduced into the airway through the cricothyroid membrane incision. This technique, however, cannot be used when the laryngeal web is thick, because the web interferes with correct insertion of the clamp. For accurate division of the web, the following surgical steps are recommended: 1) incision of the thyroid cartilage at the midline without cutting the underlying soft tissue, 2) insertion of a hypodermic needle at the supposed midpoint (anterior commissure) into the airway, and 3) fiberoptic monitoring of the needle to set it in the correct position. After the correct position of the needle is confirmed, incisions are made from the outside in, step by step along the needle guide.

Cutting the cartilage only without damaging the underlying soft tissue was realized by the use of a special knife — the ultrasonic osteotome (Sumisonic). It operates as follows. Ultrasonic waves cause the horn tip to vibrate 24,000 times per second up to a maximum of 200 μm. When the horn tip comes into contact with hard tissue, the ultrasonic vibrations are transmitted, cutting the tissue, while soft tissue absorbs vibration from the horn tip, resulting in minimal damage. The details will be given elsewhere.

Shaping Vocal Cord. In the case of a thick web, a median division of the web is not enough for the functional vocal cords to be reconstructed. How much more tissue should be excised from the vocal cord edge or subglottis can be judged under fiberoptic observation with the laryngofissure temporarily closed.

Primary or Secondary Closure of Laryngofissure. If the laryngeal web is so extensive as to cause dyspnea, it is probably better treated in two stages: the laryngofissure is closed secondarily after confirming that a sufficient airway was secured by the first operation ie, mucosa transplantation. In this two-stage operation, a pliable stent with a soft silicone cover is placed at the glottis for 10 to 14 days with the larynx kept anteriorly open until the mucosa graft takes. If no airway problem exists preoperatively, the laryngofissure can be closed primarily and the use of a stent avoided.

Assessment of Voice. The variety of surgical procedures now available for treating laryngeal webbing makes it rather difficult to choose one for an individual case. Indications must be established via comparison of the methods on the basis of objective data including a preoperative picture of the web and postoperative analysis of the voice.

CONCLUSION

Our recent experiences with rather thick laryngeal webs demonstrated that mucosa grafting, rather than skin grafting, is effective in bringing satisfactory results in both airway and voice. Precise midline division of the web is important for the success of treatment. Use of a fibrin glue is instrumental for the mucosa graft to take. Assessment of various therapeutic methods for laryngeal webbing requires objective postoperative analysis of the voice.

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TREATMENT OF INTRACTABLE ASPIRATION USING A LARYNGEAL STENT OR OBTURATOR

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Twenty-five patients were treated with a laryngeal stent for potentially reversible chronic aspiration of life-threatening magnitude. The causes of the intractable aspiration were diverse and included chronic neurologic disease, extensive head and neck surgery, and severe gastroesophageal reflux. The advantages of this technique are noted in comparison to those of more invasive procedures. Disadvantages of the laryngeal stent and complications encountered are also covered. The long-term results show that all but one patient had a significant improvement in their chronic aspiration with the stent in place. However, only eight patients achieved adequate oral deglutition without aspiration following stent removal.

KEY WORDS — aspiration, laryngeal obturator, laryngeal stent.

INTRODUCTION

Aspiration of secretions into the tracheobronchial tree occurs to some degree in all humans. This may cause immediate airway obstruction with pulmonary insufficiency and death, or may be of no clinical significance. Aspiration of material into the lower respiratory tract may occur in multiple separate events over a period of time. In these cases there is often a delay in diagnosis. The result is usually recurrent and intractable pneumonitis that may be extremely debilitating.

This paper describes our experience at Indiana University Medical Center from August 1980 to August 1990 using an obturating laryngeal stent for the treatment of clinically significant intractable aspiration. Twenty-five patients were treated in this manner. All were seriously ill as a consequence of their aspiration and usually required care in an intensive care unit. Many other patients with demonstrable aspiration, but of a less significant degree, were treated by more conservative means. The underlying cause of aspiration should be potentially reversible or a more permanent therapeutic solution should be selected.

TECHNIQUE

The stent was inserted endoscopically under general anesthesia in 23 patients. In 2 patients the stent was inserted under general anesthesia but through a laryngofissure. One of these patients had instability of the cervical spine secondary to a recent cervical laminectomy and the other patient had immobility of the cervical spine secondary to rheumatoid arthritis, prohibiting endoscopic visualization of the larynx. If a patient's medical condition does not permit general anesthesia, then insertion via laryngofissure can be easily performed with local anesthesia.

Tracheotomy is performed if this has not been previously accomplished. The endoscopist visualizes the glottis and subglottis. The neck is sprayed with an iodine-containing solution, and a beveled 14-gauge Deseret intracatheter needle is inserted approximately 1.5 cm subglottically by an assistant. The bevel is rotated so that it faces the endoscopist. Two Prolene sutures (size 2) are advanced through the needle until they can be grasped with laryngeal forceps by the endoscopist (Fig 1). Positioning the needle so that the bevel faces the endoscopist facilitates this maneuver. The Deseret needle is removed and the two Prolene sutures are clamped at each end with a hemostat. A third No. 2 Prolene suture is

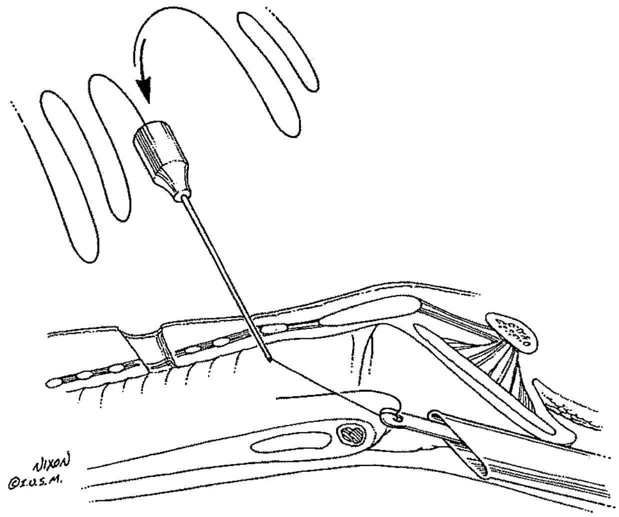

Fig 1. Two Prolene sutures are advanced through needle until they can be grasped with laryngeal forceps by endoscopist.

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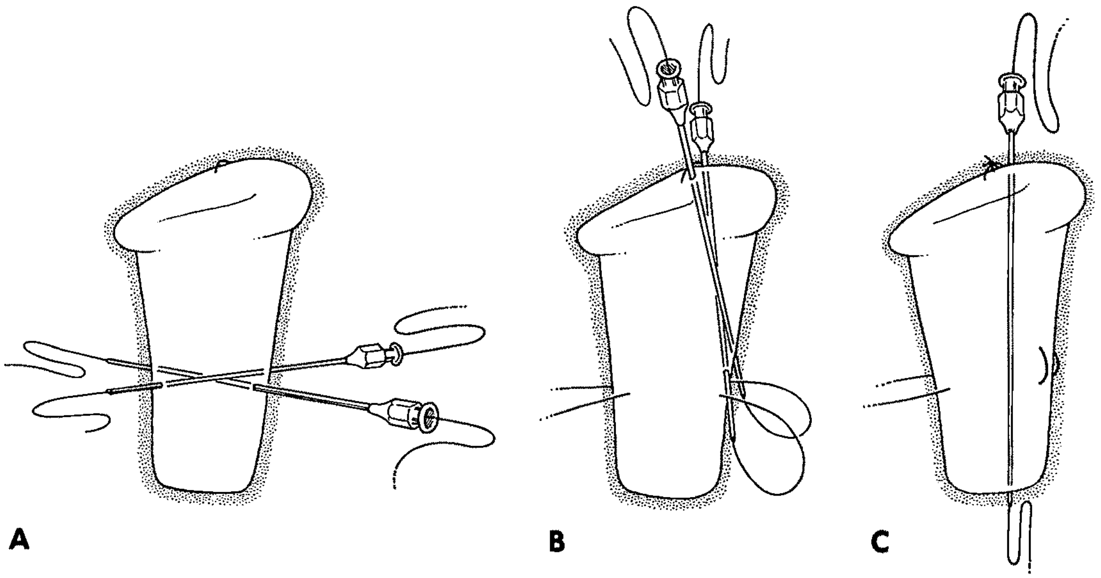

Fig 2. A,B) Two Prolene sutures are crisscrossed through stent and tied on its superior aspect. C) Third Prolene suture is passed through stent parallel to its long axis.

introduced through the tracheotomy site with a hemostat (the tracheotomy tube is temporarily removed) and is retrieved from above with endoscopic forceps. A single hemostat is clamped to each end of this suture. The laryngoscope is removed.

By means of two 18-gauge spinal needles, the percutaneously placed Prolene sutures that have been brought through the glottis and out of the mouth are crisscrossed through the stent and tied at the point at which they exit the superior aspect of the stent (Fig 2A,B). The stent is made of medical-grade silicone of intermediate firmness. (If the silicone is too hard it is unnecessarily difficult to pass sutures through the stent. Silicone that is too soft may fracture during passage of the sutures.) A stainless steel wire is incorporated into the stent with a loop exiting on the superior aspect of the stent. This loop facilitates the eventual removal of the laryngeal obturator. The stents were made by the Maxillofacial Prosthodontics Department. Several sizes should be available so that the stent fits snugly, but not extremely tightly, into the laryngotracheal area. The crossed Prolene sutures should enter the stent anteriorly at a point that would position the stent with its upper end protruding just above the level of the false vocal cords. The third Prolene suture that was introduced through the tracheotomy site is passed through the stent parallel to its long axis and is grasped by a hemostat at the point at which it exits the top of the stent (Fig 2C). This suture is used to pull the stent into the larynx and upper trachea (Fig 3). The surgeon's fingers are used to guide the stent during this maneuver and to keep it from rotating. Once the stent is in position, the guiding suture is removed by releasing the hemostat and pulling from below through the tracheotomy site. The remaining Prolene sutures that were passed through the anterior neck skin, through the anterior tracheal wall, and through the stent are threaded through a bolster button made of silicone and tied (Fig 4). These sutures anchor the stent and maintain its position.

The correct position of the stent is verified endoscopically from above. At the time of stent removal the Prolene anchoring sutures are cut after the endoscopist has exposed the stent and grasped the retrieval loop on the superior surface. The ventilating tube in the tracheotomy site should remain in the airway during this retrieval process so that there is no chance for the stent to be displaced into the proximal trachea.

Postoperative care includes routine hygiene of the tracheotomy site and daily cleansing around the anchoring button with swabs moistened with 3% hydrogen peroxide. After meals, a glass of water should be swallowed to wash food particles off the superior portion of the stent that protrudes above the glottis.

RESULTS

The causes of intractable aspiration in our series can be classified into the categories shown in the Table. Often there were secondary factors that interacted with the primary cause of intractable aspiration and magnified the morbidity. The patients who exhibited vocal cord paralysis were also septic and required ventilatory assistance using a tracheotomy or endotracheal tube. Isolated vocal cord immobility in an otherwise healthy patient can usually be managed by more conservative phonosurgical techniques.[1] A number of patients in the other categories had tracheotomy or endotracheal tubes at the time intractable aspiration was diagnosed as the cause for their pneumonia. The presence of these tubes can significantly contribute to the tendency to

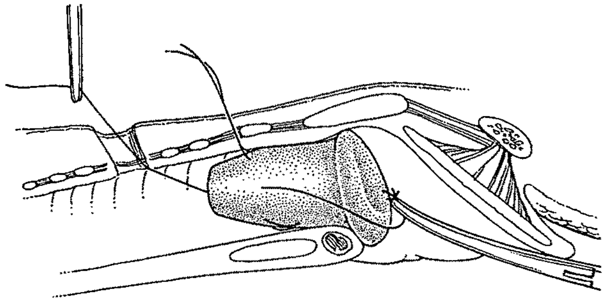

Fig 3. Prolene suture that courses parallel to long axis of stent is grasped by hemostat at superior aspect of stent. This suture is used to pull stent into larynx and upper trachea. Stent is anchored by means of silicone button and two percutaneously placed Prolene sutures.

aspirate.

The results of therapy are summarized as follows. In 24 of 25 cases, stenting resulted in reduction of the aspiration to the point that the pneumonitis cleared. In 2 cases the original stent had to be replaced with a slightly larger stent to effectively abort aspiration. A third patient had a larger stent placed but continued to aspirate and required a laryngectomy. Eight patients were able to establish adequate deglutition by mouth after removal of the stent. Five patients are alive with no significant aspiration but continue to have the stent in place. Four of these patients have achieved adequate oral intake without aspiration. One additional patient had the stent removed but still requires a gastrostomy for feeding. He is able to handle his own oropharyngeal secretions but aspirates if he attempts oral intake.

Five patients died with the stent still in place. One death was related to the surgical therapy in that demise was secondary to obstruction of the tracheotomy tube while he was at a nursing home. None of the deaths were related to continuing aspiration. Six patients continued to aspirate after stent removal and had a total laryngectomy performed.

We did experience several complications. Three patients continued to aspirate after the initial stent was placed. Placement of a larger stent solved the problem in two of these cases. One patient had a transient small laryngocutaneous fistula that occurred after laryngofissure and that responded to conservative therapy. One patient had bleeding from the anterior tracheal wall in the immediate postoperative period at the site at which the anchoring Prolene sutures perforated the anterior tracheal wall. This was corrected by endoscopic cautery after the stent was removed. Another stent was reinserted at the same time without further problems. One patient died 1 month postoperatively as a result of obstruction of the tracheotomy tube.

In one case, during endoscopic removal of the stent, breakage of the incorporated silk suture loop placed to facilitate stent removal occurred and the stent became lodged in the distal trachea. This resulted in immediate high-grade airway obstruction. The stent was pushed into the right main stem bronchus so that ventilation of the patient could be accomplished. The stent was then removed in several pieces through the tracheotomy site.

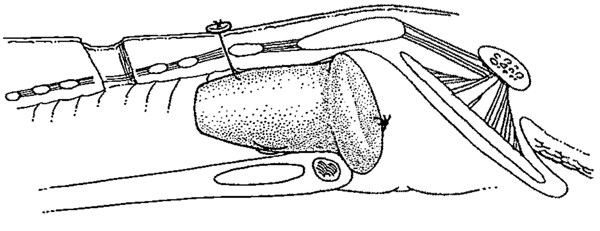

Fig 4. Two Prolene sutures that were passed through anterior tracheal wall are threaded through bolster button and tied.

CASE REPORTS

Case 1. A 4-year-old girl had a subtotal resection of a large posterior fossa ependymoma at age 2. The tumor continued to enlarge and the presence of multiple cranial neuropathies caused a severe compromise to deglutition with intractable aspiration and pneumonitis. Placement of a tracheotomy tube helped in maintaining pulmonary toilet but aspiration continued. A laryngeal stent was placed endoscopically and radiotherapy of the posterior fossa was administered. Significant resolution of the neoplasm was demonstrated on computed tomography and by clinical improvement in her cranial neuropathies. The stent was removed and deglutition by mouth was accomplished without aspiration or pneumonia. After 1 year, enlargement of the tumor with worsening of her cranial neuropathies occurred and recurrence of aspiration was noted. The stent was reinserted and chemotherapy administered. Again, a significant clinical response was noted and the stent was removed. Oral intake was again reinstituted, without aspiration. This case shows the ability to reverse and reinstitute laryngeal obturation as the clinical situation dictates.

Case 2. A 42-year-old woman presented with severe Guillain-Barré syndrome with bulbar involvement. Minimal, ineffective, and discoordinated pharyngeal propulsion was evident on the second phase of swallowing on modified barium swallow study. Laryngeal obturation with a stent was accomplished endoscopically. One year later an improvement in pharyngeal motility was demonstrated on modified barium swallow study. The laryngeal stent was removed and oral feedings were gradually reinstituted in the hospital under observation by one of our speech therapists with a special interest in problems of deglutition. Peroral intake without aspiration was accomplished without evidence of clinically significant aspiration or pneumonia.

Case 3. A 70-year-old man had a cerebral vascular accident with bulbar and cranial nerve involvement. He spent 5 weeks in the intensive care unit

CAUSES OF INTRACTABLE ASPIRATION

	No. of Patients
Neuromuscular disease	
Cerebrovascular accident	5
Mental retardation with cerebral palsy	2
Status post resection of central nervous system neoplasm	2
Guillain-Barré syndrome	2
Severe gastroesophageal reflux	
Secondary to esophagectomy	3
Secondary to gastric surgical procedure	2
Secondary to large hiatal hernia	1
Status post major ablative procedure in laryngopharynx	5
Laryngeal incompetence	
Vocal cord paralysis	1
Marked senile bowing of vocal cords	1
Cricoarytenoid joint fixation secondary to rheumatoid arthritis	1

because of sepsis and recurrent gram-negative pneumonia felt to be secondary to chronic aspiration. A laryngeal stent was inserted endoscopically. His pneumonia resolved and he was discharged from the hospital. He was able to eat by mouth without aspiration and gained approximately 11 kg (25 lb). Clinically, he seemed much stronger, and on modified barium swallow study his pharyngeal motility appeared to be improved. Four months after its placement the laryngeal stent was removed. Aspiration was noted to occur on peroral intake and infiltrates were noted on chest radiography. The stent was reinserted endoscopically. Laryngectomy was recommended but the patient refused to have the stent removed. The stent remained in place for an additional 2 years. The patient continued to do well, with adequate oral intake without aspiration. Because the patient had some occasional granulations occurring around his tracheostoma, he eventually consented to laryngectomy. At the time of laryngectomy, very minimal granulations were noted where the Prolene sutures passed through the anterior tracheal wall in the upper trachea, and at the anterior commissure. Although laryngeal obturation is not intended to be a long-term solution to intractable aspiration, this case shows that the presence of a silicone stent for more than a year does not cause significant adverse sequelae to the larynx and its mucosa.

DISCUSSION

Several factors determine the clinical significance of aspiration of material into the tracheobronchial tree. The pH, the quantity and virulence of bacteria in the aspirated material, and the presence of food particles affect the impact on the pulmonary tract.[2-8]

Other important factors are host resistance; the presence of a nasogastric, endotracheal, or tracheotomy tube; coexisting neurologic and neuromuscular disease; lower gastrointestinal disease; nonneurologic processes that compromise laryngeal competence; and epidemiologic factors.[9-25]

The diagnosis that aspiration into the tracheobronchial tree has occurred is not difficult when a single event involving massive aspiration of gastric contents or food occurs. In contrast, the diagnosis of chronic intractable aspiration as a cause for pulmonary infection rests heavily on a high index of suspicion in the susceptible host. The radiographic findings depend somewhat on the position of the patient at the time aspiration occurs. Hospitalized patients who are seriously ill are often in the recumbent position and involvement of the posterior segments of the upper lobes and the superior basal segments of the lower lobes is seen on chest radiography.[2] Observation of the act of swallowing by the physician or nursing staff often documents aspiration. Passage of oropharyngeal secretions into the glottis and upper trachea can be visualized with the fiberoptic laryngoscope. Placement of a colored indicator material into the oral cavity is soon identified in tracheal secretions of the seriously ill intubated patient who aspirates.[26] Indicator materials may also be placed in enteral feeding formulas and monitored in secretions recovered from the tracheobronchial tree.[27] Contrast radiographic studies of the act of deglutition (modified barium swallow study) can be used to document the presence of aspiration and to study its specific mechanism in a particular patient.

There is a wide spectrum of therapeutic options in treating chronic aspiration with pneumonia. Certainly, prophylactic measures are important. Evaluation by a speech therapist skilled in the area of dysphagia may be very helpful. A change in food consistency is often helpful. Clues to the correct consistency are often gained from review of a modified barium swallow study. If significant cricopharyngeal muscle dysfunction is identified as a cause of pooling in the hypopharynx, cricopharyngeal myotomy may be of benefit.[28] The use of nasogastric tubes should be minimized, and when necessary, a soft tube should be employed. Elevation of the head of the bed for surgical procedures can diminish gastroesophageal reflux. Some patients can handle their oropharyngeal secretions but cannot manage food intake by mouth. The institution of enteral feeding may significantly diminish aspiration in these cases. When enterostomy feedings are necessary the avoidance of gastric distention and oversedation is important in preventing aspiration.

When these conservative measures fail, a number of more invasive surgical therapeutic options have been described.[29,30] These include placement of a cuffed tracheotomy tube, supraglottic laryngeal closure,[31,32] glottic closure[33] and obliteration,[34] subglottic closure with laryngotracheal separation,[35] laryngeal diversion into the esophagus,[36-38] and total laryngectomy.[39] We have employed an additional surgical option — laryngeal obturation with a stent.[40] Placement of a cuffed tracheotomy tube often does not preclude aspiration. As previously mentioned, the presence of a tracheotomy tube inhibits the up-and-down motion of the larynx on swallowing and predisposes to aspiration. Inflation of the tracheotomy tube cuff obstructs passage of material into the middle and lower esophagus and promotes pooling in the hypopharynx.[41] Food and secretions may collect above the cuff, only to be periodically aspirated as a bolus when the patient's position is changed or the cuff is deflated. The other surgical alternatives to laryngeal obturation involve creation of a significant wound in a patient who is often seriously ill and malnourished, with consequent impairment of the immune response and wound-healing capacities. All except total laryngectomy are potentially reversible but involve a significant secondary surgical procedure that essentially amounts to a laryngotracheal reconstruction.

Correction of aspiration by laryngeal obturation with a stent has a number of significant advantages. It can usually be accomplished endoscopically without the creation of a wound. It is easily reversible by simply removing the stent. We have encountered no significant injury to the upper airway secondary to stenting. A small amount of granulation tissue is seen on the anterior tracheal wall where the anchoring sutures were located. This has never been of clinical significance and no cases of airway stenoses have been observed. Four patients had the stent in place for over 1 year, and even with prolonged stenting no laryngotracheal injury or stenosis has been noted. Unlike a tracheotomy or endotracheal tube, the stent moves with the larynx on deglutition and the shearing action on the mucosa is avoided. The stent is made of medical-grade silicone, which is biologically inert. A size of stent is selected that fits snugly into the larynx and upper trachea but does not exert extreme pressure on the mucosa.

Disadvantages of laryngeal stenting for the treatment of chronic aspiration do exist. There is usually no effective vocalization, although Eliachar et al[42] have developed a stent that is hollow, with a superiorly located slit through which vocalization can occur. There is no definitive test to decide when the stent can be removed; however, the same can be said about the timing of reversal of the other surgical therapeutic options. Should the clinical perception that the stent can be removed be incorrect, it is simple to reinsert the obturator, whereas it would be prohibitively difficult to again perform the other surgical operations.

Our indication for employing a laryngeal stent to correct intractable aspiration pneumonia is a seriously ill patient with evidence of chronic aspiration in whom the cause of aspiration is potentially reversible. Also, the patient should have the potential for recovering useful speech. Documented aspiration that is less clinically significant can be treated by more conservative measures. If the cause of aspiration has no hope of being corrected, or if the patient will never have a capacity for useful speech, total laryngectomy is the most definitive solution.

Probably the most challenging problem is deciding when the stent is to be removed. Some improvement in the causative factors resulting in aspiration must be perceived to have occurred, such as recovery of pharyngeal function after a neurologic insult. This can sometimes be documented on a modified barium swallow study. However, the final test is "by fire," ie, the stent is removed and the patient is observed for signs of aspiration or pneumonia. If aspiration or pneumonia recurs, the stent can be reinserted or a more definitive solution such as laryngectomy can be performed.

Certain aspects of the technique of stent insertion deserve detailed scrutiny in order to avoid complications. The size and position of the stent are important. Maxillofacial prosthodontists are skilled and experienced at fabricating prostheses from medical-grade silicone. They provide us with a range of stent sizes that are available in the operating room. The manufactured laryngeal stent made by Hood Laboratories (Pembroke, Mass) serves as a model and can itself be used for obturating the larynx. The size of the laryngeal stent for men is 15 mm in width, 20 mm in anterior-posterior width, and 45 mm in length. A laryngeal stent for women is correspondingly 12 x 15 x 36 mm. These sizes are usually appropriate for average adult male and female patients, respectively. However, certain features of these manufactured stents are less than optimal. They are made of a very soft silicone material that easily cuts and fragments if subjected to any shearing forces. A laryngeal stent made by Boston Medical Products (Waltham, Mass) is manufactured from a firmer grade of silicone and is less likely to fragment. The silk suture embedded in the stent and used for retrieval is more likely to break than an embedded stainless steel wire loop. The latter is also radiopaque. If laryngeal obturation is to be used in a pediatric patient it is even more important that a variety of sizes be available. The distal end of the stent should taper slightly to facilitate its endoscopic introduction into the laryngotracheal area.

The stent should be positioned so that the superior aspect protrudes just above the level of the false vocal cords. The stent serves as a "watershed" directing solid material into the esophageal introitus. It is not wedged so tightly into the larynx that materials cannot pass by it. In one of our cases the stent was positioned so that its superior aspect was below the level of the true vocal cords. This allowed pooling to occur above the stent and required repositioning to prevent aspiration. If the upper end of the stent is positioned too far cranially, the epiglottis, if present, is propped forward and deglutition is associated with discomfort.

During stent removal the tube inserted through the tracheotomy site and used to ventilate the patient during anesthesia should not be removed until the stent has been removed from the larynx. In the case in our series in which the stent became lodged in the distal trachea at the time of removal, the ventilating tube had been temporarily removed so that the stent could be pushed through the glottis from below. This was necessary because the silk suture incorporated in the stent had broken. Removal of the ventilating tube provided the opportunity for potentially catastrophic distal migration of the stent.

SUMMARY

A Silastic stent used as a laryngeal obturator is a very effective temporary solution to the problem of intractable aspiration with secondary pneumonia. This procedure can almost always be performed endoscopically and is easily reversible by simply removing the stent. If there is not sufficient improvement in the pathologic process causing the chronic aspiration, then pneumonia will recur after stent removal. A more definitive solution such as total laryngectomy can then be employed.

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TRANSTRACHEAL DELIVERY OF OXYGEN: EFFICACY AND SAFETY FOR LONG-TERM CONTINUOUS THERAPY

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Transtracheal (TT) oxygen delivery involves administration of oxygen percutaneously through a catheter inserted in the suprasternal trachea. Transtracheal oxygen delivery has been proposed as a means of overcoming the high visibility, inconvenience, and discomfort associated with nasal cannula use. This report describes our experience using TT delivery in 40 patients with chronic obstructive pulmonary disease (n = 32) and other types of lung disease (n = 8). Overall acceptance of TT catheter use was high and only 5 subjects elected to discontinue use. We believe the TT route is a relatively safe approach for oxygen administration and a promising method of improving patient compliance. It also offers the potential of more adequately oxygenating patients with refractory hypoxemia.

KEY WORDS — transtracheal catheter, transtracheal oxygen delivery.

INTRODUCTION

Approximately 800,000 patients in the United States are currently receiving home oxygen therapy. When used continuously, oxygen therapy offers many benefits for patients with severe hypoxemia, including improved hemodynamics, improved neuropsychological function, and decreased mortality.[1-4] Life is prolonged in proportion to the number of hours per day that oxygen is used.[1,3] However, despite the proven benefits of this therapy, many patients avoid using their oxygen continuously because of its inconvenience, discomfort, and social stigma.[5,6]

Traditionally, continuous oxygen therapy is delivered by nasal cannula. Although simple to use, this device is cosmetically unattractive. High flows delivered into the nose cause drying of the nasal mucosa with resulting sequelae of nasal crusting and blockage, dry throat, hoarseness, and epistaxis.[6] In addition, nasal delivery is inefficient. All oxygen delivered during expiration is lost to the atmosphere. Heimlich,[7] in 1982, introduced a system of transtracheal (TT) oxygen delivery through a catheter inserted percutaneously into the suprasternal trachea. Potential advantages include increased efficiency of oxygen delivery, enhanced patient compliance, and increased exercise tolerance.[7-13] This report describes our protocol and experience using TT oxygen delivery, including criteria for candidate selection, catheter insertion technique, patient management, and problems encountered.

METHODS

The sample consisted of 40 patients (29 men and 11 women) who were followed up by private physicians (25 patients) or the Veterans Administration Medical Center (15 patients) and had TT catheter insertions performed by the investigators. The mean age was 62±9 years (mean±SD), with a range of 42 to 76 years (Table 1). Of the 40, 32 had chronic obstructive pulmonary disease (COPD) and 8 (hereinafter referred to as the mixed group) had other types of hypoxemic lung disease, including idiopathic pulmonary fibrosis (3 subjects), asbestosis (1), coal worker's pneumoconiosis (1), kyphoscoliosis (1), lymphangiomyomatosis (1), and mixed connective tissue disease (1). Mean forced expiratory volume in 1 second (FEV1) was 1.07±0.71 L in the COPD group and 1.25±0.59 L in the mixed group. Time on nasal cannula oxygen delivery prior to study entry ranged from 1 to 96 months.

TABLE 1. MEAN AGE, SPIROMETRIC VALUES, AND MONTHS OF TRANSTRACHEAL OXYGEN USE

Lung Disease	*Age (y)*	*FVC (L)*	*FEV1 (L/s)*	*FEV1/ FVC*	*TT Use (mo)*
Obstructive (n = 32)					
Mean	63	2.49 (63)	1.07 (38)	43	20
SD	8	1.02 (22)	0.71 (23)	18	16
Range	42-76	1.00-4.73	0.37-3.22		0-72
Mixed (n = 8)					
Mean	55	1.69 (45)	1.25 (45)	78	4
SD	10	0.76 (21)	0.59 (16)	12	5
Range	42-73	0.73-2.83	0.55-2.35		0-14

Numbers in parentheses show percent of predicted value that was achieved.

FVC — forced vital capacity, FEV1 — forced expiratory volume in 1 second, TT — transtracheal catheter.

Transtracheal oxygen delivery was initiated by

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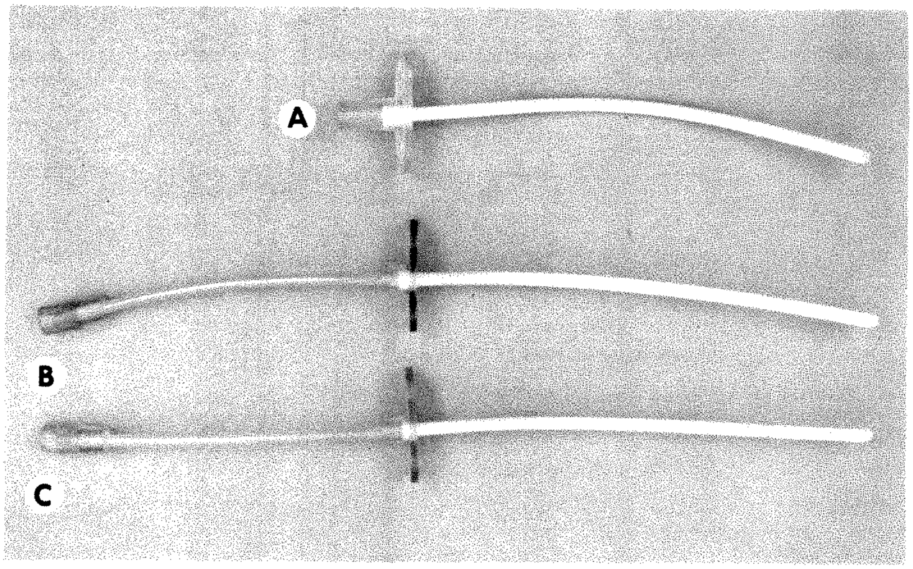

Fig 1. SCOOP system consists of three components. A) Stent used for first week after insertion to allow maturation of tract. Oxygen is not delivered through stent. B) SCOOP 1 catheter with single end hole. This is used for next 2 months. C) Multiported SCOOP 2 catheter, which may be substituted at end of this time.

means of a catheter designed for this method of oxygen delivery (SCOOP, Transtracheal Systems, Englewood, Colo) (Fig 1). The steps in initiating TT oxygen delivery generally followed those described in the SCOOP protocol.[14] Briefly, they were as follows.

Phase 1 (Evaluation and Selection). Patients initially met with a pulmonary clinical nurse specialist who discussed the procedure and determined if the patient could provide the required self-care. When possible, this discussion included the patient's spouse. Patients were also encouraged to talk with other patients currently using TT oxygen delivery. If a decision was made to use TT delivery, the procedure was scheduled after a medical evaluation by a pulmonologist. Data collected before the procedure included a history and physical examination, arterial blood gases, hematocrit, prothrombin and partial thromboplastin times, spirometry, and posteroanterior and lateral chest radiographs. Patients were selected for the TT procedure if they met the following criteria: 1) need for continuous oxygen therapy ($Pa_{O_2} \leq 55$ mm Hg while breathing room air at rest or ≤ 59 mm Hg with evidence of peripheral edema, hematocrit $\geq 55\%$, and/or cor pulmonale while receiving optimal medical therapy), 2) ability to follow instructions for care of the TT catheter, 3) no acute exacerbation present, 4) no more than 30 mg of steroids daily, 5) no evidence of a coagulopathy, and 6) no evidence of herniation of the lung over the proposed site for catheter insertion.

Phase 2 (Stent Week). The stent is a nonfunctioning tube that is sutured in place for a week following the insertion procedure (Fig 1). The purpose of the stent is to facilitate tract formation, reduce the potential of subcutaneous emphysema, and reduce postoperative coughing and discomfort. Prior studies have shown a higher incidence of coughing, throat discomfort, and subcutaneous emphysema when oxygen flow is begun immediately after catheter insertion.[11,15]

Insertion of the stent was accomplished by a team consisting of a surgeon and a pulmonary clinical nurse specialist. Whether the insertions were done in the bronchoscopy suite or the clinical unit depended on the severity of the subject's illness. Several hours prior to the procedure, subjects received 500 mg of cephalexin for prophylaxis.

During the insertion procedure, the subject was placed in a supine position. A small shoulder roll was used to produce moderate extension of the neck. Oxygen was delivered by cannula throughout the procedure. A chain (later to be used to secure the catheter) was placed around the neck to identify the point that provided maximum stability for insertion of the catheter. The chain was then removed and the cricoid cartilage identified by palpation and marked with a surgical pen (Fig 2A). The skin overlying the insertion site, usually the second or third tracheal ring, was infiltrated with 1% lidocaine hydrochloride with epinephrine. The infiltration was then carried through the appropriate tracheal interspace and the mucosa of the trachea was anesthetized with topical lidocaine. This accomplished, the skin overlying the interspace was sharply incised to make a 1-cm vertical incision. An 18-gauge thin wall needle attached to a syringe was then directed through the incision into the trachea via the interspace. The syringe was removed and a guide wire passed through the needle downward into the trachea (Fig 2A). The needle was then withdrawn. Coughing was controlled with topical lidocaine as needed. A 10F dilator was fed over the guide wire to bluntly dilate the trachea (Fig 2B). The dilator was removed and the guide wire left in place. The stent was inserted over the guide wire and the wire withdrawn (Fig 2C). The stent was sutured to the skin, and posteroanterior and lateral chest radiographs were taken to document correct

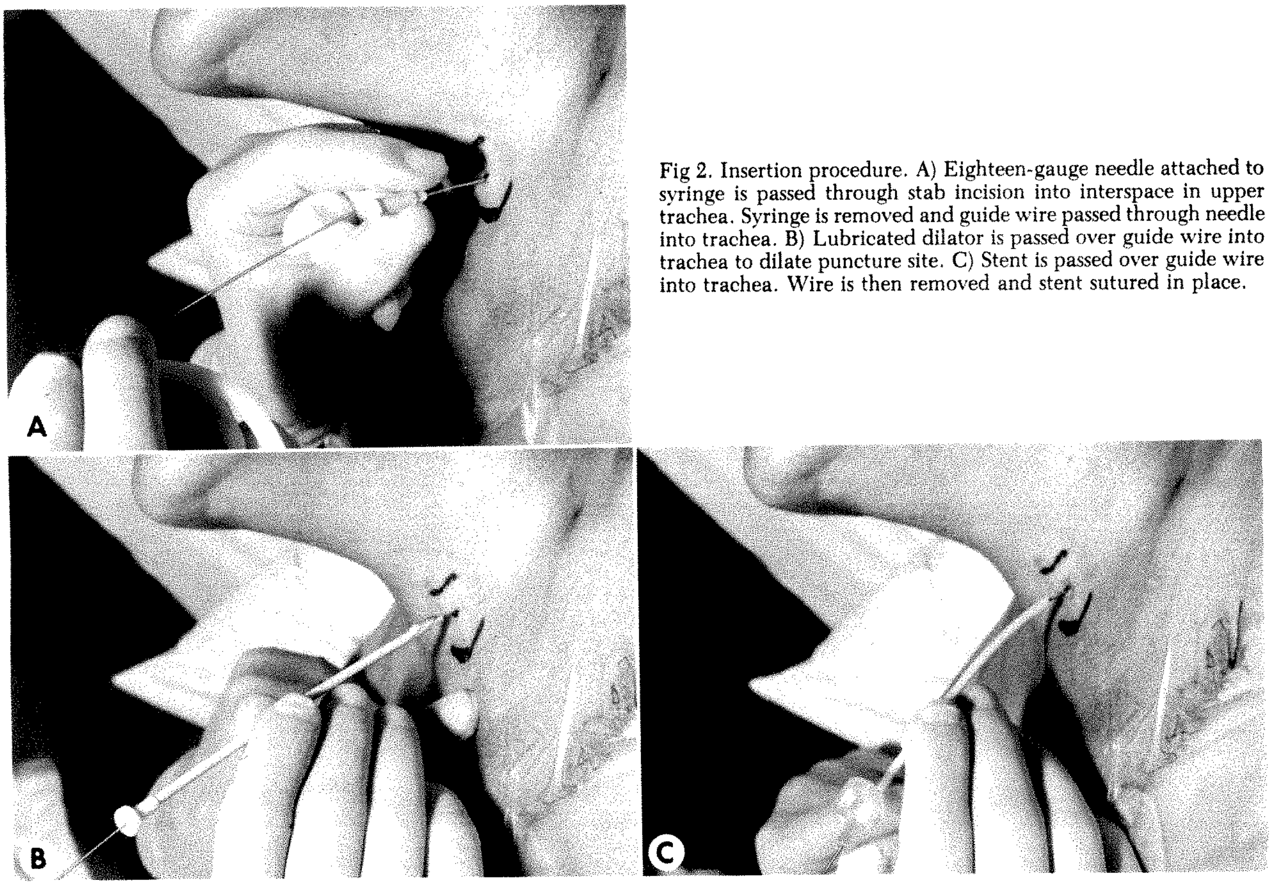

Fig 2. Insertion procedure. A) Eighteen-gauge needle attached to syringe is passed through stab incision into interspace in upper trachea. Syringe is removed and guide wire passed through needle into trachea. B) Lubricated dilator is passed over guide wire into trachea to dilate puncture site. C) Stent is passed over guide wire into trachea. Wire is then removed and stent sutured in place.

position.

Following stent insertion, subjects were instructed to take cephalexin (250 mg every 6 hours) for 7 days and advised to take guaifenesin as needed for cough. Teaching consisted of instructions to clean the site twice daily with attention to removing all crusts and to report any signs of infection or subcutaneous emphysema. Subjects were also called the first day following discharge to determine any problems.

Phase 3 (Immature Tract). One week after insertion, the stent was removed over a wire guide and a SCOOP 1 catheter (9F) inserted. This catheter has a single end port, an 11-cm intratracheal segment designed to position the catheter tip ≥ 1 cm above the carina, a flange, and a 9-cm external segment that attaches to the patient's oxygen delivery tubing (Fig 3). Flows of 6 to 8 L/min can be delivered through this catheter.

Determination of oxygen flow requirement at rest and during exercise was made by titrating the flow required to maintain an arterial oxygen percent saturation (SaO_2) of 91% to 95% (PaO_2 60 to 80 mm Hg). Arterial blood gases were drawn after 1 to 2 hours to document acid-base status. Subjects were taught to 1) clean their catheter in place two or three times daily using saline and a cleaning rod, 2) use a therapeutic cough technique to help dislodge any mucus balls that formed on the catheter,[16] 3) report signs of mucus obstruction (whistling sound from the humidifier, sudden pop when oxygen tubing is disconnected, increasing or severe cough, dyspnea, or fluid in the tubing) and to return to the clinic if these persisted so that the catheter could be cleaned by removing and reinserting it over a guide wire (stripping), 4) place two strips of tape (OpSite or EnSure) on either side of the catheter as an added precaution against accidental displacement, and 5) call immediately if the catheter became displaced from the tract and could not be reinserted. Subjects were not scheduled to return to the clinic on a routine basis for catheter stripping. Instead, progress and problems were monitored by phone calls and return visits were scheduled as needed. All care in phase 3 was the primary responsibility of the clinical nurse specialist.

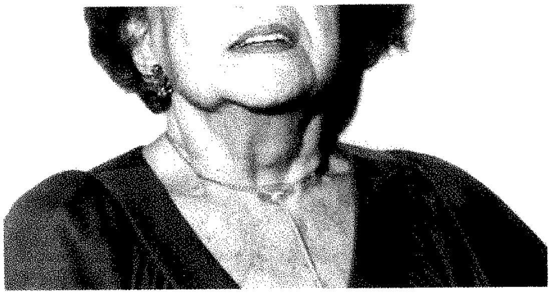

Fig 3. Transtracheal catheter in place. Oxygen is delivered through catheter directly into lungs, eliminating need for nasal cannula.

TABLE 2. OXYGEN REQUIREMENT AT REST BEFORE AND AFTER TRANSTRACHEAL CATHETER INSERTION

Oxygen Requirement	*No. of Subjects*	*Nasal Cannula*	*Transtracheal Catheter*
Adequately oxygenated*			
1 L/min	1	1.00	1.00
2 L/min	8	2.00	1.00
2.5 to 4 L/min	17	3.32 (SD = 0.53)	1.88 (SD = 0.48)
4.5 to 6 L/min	5	5.40 (SD = 0.55)	3.00 (SD = 0.61)
Refractory†			
6 L/min	3	6.00	6.00
Nonrebreathing mask or face mask (50% to 70%)	2	Not applicable	6.00
	2	Not applicable	8.00
	2	Not applicable	6.00 plus nasal cannula at 2 L/min

*PaO2 > 60 mm Hg with nasal cannula therapy.

†PaO2 < 60 mm Hg with nasal cannula therapy.

Phase 4 (Mature Tract). After 8 weeks, the subjects returned to the clinic to learn the skills required to remove the TT catheter for cleaning. Initially, removal and reinsertion were performed twice daily. The frequency was later individualized by the subject according to frequency of mucus buildup. SCOOP 2 catheters (single end port and six side ports) were initially used in this phase of care. SCOOP 1 catheters (single end port) were substituted after entry of 20 subjects, because the SCOOP 1 catheter required less frequent removal for cleaning for most subjects. Progress was monitored by twice-monthly phone calls. Primary responsibility for all care in this phase belonged to the clinical nurse specialists.

RESULTS

Oxygen Requirement. Most subjects (n = 31) were adequately oxygenated (PaO2 > 60 mm Hg) on nasal cannula delivery prior to TT catheter insertion. Three (7%) subjects had refractory hypoxemia (PaO2 < 60 mm Hg) on nasal cannula therapy at 6 L/min and six (15%) were oxygenated with higher oxygen concentrations via a nonrebreathing mask or face mask (Table 2).

Changes in oxygen requirement following TT catheter insertion are shown in Table 2. Oxygen requirement did not decrease for the subject who required 1 L/min via nasal cannula, as he could not be adequately oxygenated at 0.75 L/min by TT catheter. With this exception, oxygen flow rates decreased for all subjects who did not have refractory hypoxemia. Five subjects with refractory hypoxemia were able to be adequately oxygenated with 6 L/min by TT catheter, and two with a flow of 8 L/min. The remaining two subjects with refractory hypoxemia were oxygenated with 6 L/min through the catheter and 2 L/min by nasal cannula. This combination, rather than 8 L/min by TT catheter, was used initially in phase 3 because both subjects were steroid-dependent and thus judged at greater risk for subcutaneous emphysema.

TABLE 3. PROBLEMS ENCOUNTERED DURING TRANSTRACHEAL OXYGEN DELIVERY IN 40 SUBJECTS

Problem	*No.*	*%*
Stent week		
Paroxysmal coughing	2	5
Bronchospasm	1	2
Immature tract (1 to 2 mo)		
Symptomatic mucus balls*	10	25
Catheter displacement		
Accidentally displaced from tract	9†	22
Investigators unable to reinsert (lost tract)	3	7
Probable bacterial cellulitis	3	7
Subcutaneous emphysema	2	5
Hemoptysis (>5 mL)	2	5
Cephalad-displaced catheter	1	2
Severed catheter	1	2
Mature tract (>2 mo)		
Catheter displacement		
Removed to clean, patient unable to reinsert	9	22
Investigators unable to reinsert (lost tract)	3	7
Keloid formation	3	7
Probable bacterial cellulitis	2	5
Contact dermatitis	1	2
Duration of use		
Continued use	34	85
Subject elected to discontinue	5	13
Investigators discontinued	1	2

*None in 14 subjects since using OpSite.

†Required catheter removal over wire for resolution (stripping).

Stent Week. Minimal problems were experienced during the stent week (Table 3). The most common constellation of responses was a "tickle cough" relieved by use of guaifenesin, scant hemoptysis, and minimal discomfort at the puncture site. Two subjects developed paroxysmal coughing that could not be controlled with oral cough suppressants. Both were instructed to inject 0.5 mL of 1% lidocaine hydrochloride into their stent every 4 to 6 hours as needed for 24 hours; this treatment relieved the coughing. One subject experienced an episode of bronchospasm after the insertion procedure that resolved with treatment by nebulized metaproterenol sulfate.

Immature Tract. During this phase, subjects experienced the most problems. The most frequent resulted from inspissation of mucus in the airway and the formation of mucus balls on the catheter. Thirty (75%) of the subjects were successfully able to cough these up by using the previously described cleaning and cough technique. Mucus balls were detached for the remaining 10 subjects by inserting a wire through the catheter, removing the catheter over the wire, and cleaning and reinserting it. Large symptomatic mucus balls were seen more frequently in subjects requiring higher flows (≥4 L/min) and during the initial 4 weeks of catheter use.

One subject, who required 4 L/min by TT catheter, experienced a partial upper airway obstruction from a large inspissated mucus ball coincidental with hospitalization. Even though the mucus ball was expectorated, the episode of obstruction aggravated the subject's severe respiratory insufficiency. The subject died after an extended period of hospitalization and mechanical ventilation.

Nine subjects accidentally displaced their catheters, typically at night. This was an emergent problem because the tract may close within 1 to 2 hours, preventing catheter reinsertion. Reinsertion was accomplished by first attempting to insert a lubricated guide wire into the tract. If insertion was successful, the catheter was inserted over the wire. If the tract could not be identified, skin anesthesia and insertion of a 10F dilator (supplied with the insertion kit) was attempted. Five catheters were successfully reinserted with a guide wire and one with a dilator. Reinsertion was not successful for the remaining three subjects and a second insertion procedure was performed. We then began advising the subjects to apply two small strips of Opsite or Ensure on either side of the catheter flange for the initial 2 weeks of SCOOP 1 use. No accidental displacements have occurred during the initial 2 months of TT use since this approach was implemented (14 subjects).

Three subjects experienced a probable bacterial cellulitis 2 to 4 weeks after the prophylactic regimen ended. This resolved with treatment by oral antibiotic therapy. Two subjects experienced subcutaneous emphysema. One was obese and the second had diabetes mellitus and was steroid-dependent. This problem was managed by delaying catheter hookup for an additional 2 weeks. Two subjects experienced hemoptysis (>5 mL). Bronchoscopy in one individual of short stature (155 cm) revealed mucosal erosions at the carina and orifice of the right main stem bronchus. Hemoptysis resolved after substitution of a shorter catheter. Hemoptysis in the second subject was self-terminating and did not result in respiratory compromise. However, the subject elected to discontinue TT use. Also, one patient experienced a cephalad-displaced catheter.

One equipment-related problem was encountered. The external portion of a SCOOP 1 catheter was inadvertently severed during an observational visit by a home care worker not familiar with the SCOOP system. The internal portion of the catheter remained intact and the catheter was replaced without further problems. No subjects experienced problems with catheter breakage.

Mature Tract. During extended TT use, nine subjects experienced an episode of being unable to reinsert their catheter after removing it for cleaning. In six instances, the investigators were able to reinsert the catheter using a guide wire (four subjects) or dilator (two). Reinsertion was not successful for the remaining three subjects and a second insertion procedure was performed. Subsequently, three of these subjects elected to return to the clinic for catheter changes. The remainder continued to remove and reinsert their catheters at home for cleaning.

Three subjects experienced keloid formation at the insertion site. This was managed by steroid injection (two subjects) or excision (one). Two subjects experienced a probable bacterial cellulitis that resolved with oral antibiotic therapy. One subject experienced an episode of contact dermatitis when using the bead chain. The dermatitis resolved with treatment with topical steroids and substitution of a gold chain.

Duration of Use. Subjects with COPD were followed up for 629 months of TT use (mean, 20±16 months; range, 0 to 72 months), and subjects in the mixed group for 29 months (mean, 4±5 months; range, 0 to 14 months) (Table 1). Eighteen subjects died while using TT delivery: 11 of 32 in the COPD group and 7 of 8 in the mixed group. All subjects in the mixed group died of causes related to progression of their underlying lung disease. Subjects with COPD died as a result of disease progression or other unrelated causes. No deaths were directly attributed to complications of the TT catheter.

Five subjects elected to discontinue use of TT delivery (Table 3). Reasons were dislike of the delivery method (three subjects), concern because of hemoptysis (one), and severe arthritis resulting in limited mobility (one). In addition, the investigators discontinued catheter use for one subject who required extended hospitalization.

DISCUSSION

With TT delivery, oxygen enters the trachea directly. Thus, it usually permits adequate arterial saturation with flow rates that are lower than those used with nasal cannula delivery. Of the 31 subjects who were adequately oxygenated with nasal delivery, 30 (97%) decreased their flow rates. The reduction ranged from 25% to 50%. Similar results have been reported by others.[8,9]

Nine subjects had refractory hypoxemia. Seven of these achieved a Pa_{O_2}> 60 mm Hg at rest with TT delivery using flows ranging from 6 to 8 L/min. Christopher et al[10] reported similar success in oxygenating severely hypoxemic subjects. To prevent the complication of subcutaneous emphysema, a decision was made to oxygenate the remaining two subjects (both steroid-dependent) with 6 L/min by TT catheter and 2 L/min via cannula. Although this approach did not resolve their dependence on nasal delivery, it improved oxygenation and permitted discharge from the hospital setting.

An additional advantage of TT delivery is the ability to promote continuous (24-hour) oxygen use, an outcome associated with a significant reduction in mortality.[1] Transtracheal delivery also eliminates problems related to use of the nasal cannula such as nasal crusting and blockage, dry throat, hoarseness, and epistaxis.[6]

Although TT delivery is an invasive procedure, adverse events were not common and did not discourage most subjects (34 of 40) from continuing its use. This outcome is in contrast to our previously reported experience, in which more problems were encountered and a greater number of patients (5 of 10) discontinued TT use.[11] Our prior experience with TT delivery involved use of a TT catheter assembled by positioning a 16-gauge angiographic catheter through a 3.5-mm reversed pediatric tracheostomy tube. Oxygen delivery was initiated immediately after insertion, resulting in a high incidence of subcutaneous emphysema.[15] Also, the small size of the angiographic catheter prevented delivery of flows >2.5 L/min. High flows led to buildup of pressure in the humidifying system and leakage from the pressure relief valve.

We elected to use the SCOOP system because it incorporated mechanisms designed to offset these problems. The stent week facilitated preventing subcutaneous emphysema. The larger SCOOP catheter can accommodate flows of 6 to 8 L/min, facilitating treatment of patients with refractory hypoxemia.

With use of the SCOOP system, the type and frequency of problems vary with the phase of introduction. Two problems were seen during the stent phase: paroxysmal coughing in two subjects and bronchospasm in one subject. Both were relieved by symptomatic treatment. No subjects experienced procedure-related complications, subcutaneous emphysema, or stomal infections. Christopher et al[9] reported subcutaneous emphysema in 3% of their subjects and acute bronchospasm in 2%. From a series of 22 subjects, Adamo et al[17] reported one episode (5%) of a misplaced catheter entering the anterior mediastinum during the insertion procedure and stomal infections in 6 subjects (29%), despite use of prophylactic antibiotics (cefaclor or cephalexin). All subjects in our study received detailed teaching and reinforcement by phone regarding the need to clean the stent site twice daily with cotton swabs and hydrogen peroxide — a factor that may have decreased infectious complications.

Most problems occurred during the period in which the tract was immature and the catheter was cleaned in place. Ten (25%) subjects required catheter removal over a wire to displace mucus balls that had formed on the catheter tip. This incidence compared with one of 10% to 14% reported in other series in which the SCOOP system was used.[9,17] Possibly, this higher incidence resulted from a larger number of subjects with refractory disease included in this series.

A mucus ball is an accumulation of inspissated mucus that adheres to the outside of the catheter just above the tip.[14] Factors involved in formation include the volume of dry gas introduced into the airway, the effectiveness of the cough, and the volume of secretions. Inadequate humidification and ineffective cleaning may also predispose patients to this problem. Symptomatic mucus balls occur when subjects cannot dislodge the mucus by cleaning or using a therapeutic cough technique.[14,16] Mucus balls may cause airway obstruction. Adamo et al[17] and Fletcher et al[18] reported one episode each of airflow obstruction resulting from inspissated mucus collecting on the catheter tip. Neither could be related to a lapse in catheter-cleaning technique or humidification. Both cases were resolved without complications following bronchoscopy removal or catheter removal. In our study, one subject also experienced a partial upper airway obstruction from a large inspissated mucus ball.

Catheter removal typically resolves problems related to mucus obstruction, because mucus is stripped from the catheter as it leaves the tract. For this reason, mucus balls are less problematic in phase 4, when the tract is mature and the catheter can be removed daily for cleaning.

The current SCOOP protocol recommends that all subjects have their SCOOP 1 catheter removed 1 week following insertion to assess mucus buildup.[14] Instead of weekly stripping, we followed subjects by phone calls. Return to the clinic or home visits were initiated if the previously noted symptoms of mucus obstruction were reported. This approach, rather than periodic return visits, was used because travel to the clinic was difficult for some subjects. Our approach was successful in preventing complications related to mucus balls in all but one subject.

In addition, nine (22%) subjects experienced accidental catheter displacement in phase 3, most frequently at night. Christopher et al[9] reported a 7% incidence of catheter displacement in phase 3. Adamo et al[17] reported a 33% incidence of displacement, also typically at night. As noted previously, displacement has not been a problem since we began advising the subjects to apply tape (Opsite, Ensure) on either side of the catheter flange for the initial 2 weeks of SCOOP 1 use.

In phase 4, the most common problem was difficulty reinserting the catheter after removal for cleaning. This problem has been attributed to development of scar tissue or keloids. Factors that are believed to predispose to this problem include cricothyroid membrane puncture, exposure of cartilage during the procedure, excessive catheter removal for cleaning (more than twice a day), and patient predisposition.[14] Other researchers[17] have also noted this problem. When reinsertion continued to be a problem, we instructed subjects to clean the catheter in place (as during phase 3) and return to the clinic at 3-month intervals for placement of a new SCOOP catheter.

Because TT delivery requires active participation of the patient, the most important step in implementing TT oxygen delivery is patient teaching. Particular attention should be paid to describing the required self-care and determining if the candidate is capable of following the required regimen and has realistic expectations of its benefits. The skills required in caring for a TT catheter are not difficult to learn if sufficient time is spent in patient education.[7-14,16] Time spent in this phase can help to identify subjects who are the most appropriate candidates and thus likely to continue using the therapy. Detailed teaching regarding the required care is essential.

Candidates who elect to use TT oxygen delivery can be divided into two broad categories: those adequately oxygenated on nasal cannula delivery and those with refractory hypoxemia. Greater demands are placed on the health care team in terms of management for candidates who require flows ≥6 L/min on nasal delivery, especially if they are in a rapid, potentially preterminal, phase of escalating oxygen requirements. Transtracheal oxygen delivery may permit a higher quality of life in such patients because it allows adequate oxygen delivery without use of a face mask or nonrebreathing mask. However, this benefit may be short-term owing to progression of the underlying lung disease. A decision to offer TT delivery in such patients must be realistically evaluated in terms of potential benefits to the patient and family. Special consideration needs to be given to determining the benefits TT delivery can offer relative to progression of the underlying lung disease.

Of the refractory subjects managed in this study, three were using nasal cannula delivery at 6 L/min and required TT oxygen delivery at 6 L/min. Two of these subjects used TT delivery for 17 and 20 months while ambulatory and managed on an outpatient basis. Their hypoxemia then progressively increased, resulting in acute respiratory failure and death. The third subject continues to use TT at 15 months after insertion, is ambulatory, and has not been hospitalized since his catheter insertion.

Outcome was more problematic for the six subjects who were using oxygen by face mask prior to TT delivery. Oxygen requirements steadily increased. Three of these subjects used combinations of TT delivery, TT and nasal cannula delivery, or TT and face mask delivery for periods of 8, 6, and 2 months before dying of complications of their lung disease. Two of the remaining subjects died suddenly at home within 1 month of TT catheter use and the third elected to discontinue use.

In summary, this experience with 40 subjects using TT delivery confirms our previous observations regarding the relative safety and efficacy of TT use. Although some problems were encountered, most were minor and confined to the initial phase of TT delivery, in which the tract is immature and the catheter must be cleaned in place. Those problems did not dissuade most subjects from continuing TT catheter use. In fact, they actively promoted this approach to oxygen delivery when speaking with potential candidates for its use. We attribute the reduction in serious problems and resulting increase in patient acceptance encountered in this recent experience with TT delivery to a better understanding gained in our initial study. This improvement highlights the need for providers of this form of oxygen delivery to become thoroughly familiar with all aspects of the technique and to provide adequate support and teaching before offering this service.

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MAJOR ADVANCES IN ONCOLOGY: UPDATE ON CANCER OF THE HEAD AND NECK

The Ireland Cancer Center and the Department of Otolaryngology–Head and Neck Surgery, University Hospitals of Cleveland and Case Western Reserve University School of Medicine, will present a symposium entitled Major Advances in Oncology: Update on Cancer of the Head and Neck, to be held March 1-2, 1991. For further information, contact Education Coordinator, Ireland Cancer Center, University Hospitals of Cleveland, 2074 Abington Road, Cleveland, OH 44106; (216) 844-7858.

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SURGICAL APPLICATIONS OF ULTRATHIN FLEXIBLE BRONCHOSCOPES IN INFANTS

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Ultrathin flexible bronchoscopes with controlled distal angulation allow the conventional diagnostic examination of the lower airways of even the smallest infants. These instruments may be passed through small endotracheal or tracheostomy tubes while ventilation is maintained. It is thus possible, under direct visualization, to control the manipulation of surgical instruments where they could not otherwise be seen, or to study airway dynamics and anatomy intraoperatively without extubating the patient.

KEY WORDS — bronchoscopy, infants, ultrathin flexible bronchoscope.

INTRODUCTION

The care of infants with airway disease presents many challenges to physicians, not the least of which is the difficulty in examining and manipulating the lower airways. Advances in endoscopic techniques and instrumentation in the past two or three decades have included the glass rod telescope[1] and increasing miniaturization of flexible bronchoscopes.[2-7] These new instruments have significantly facilitated bronchoscopy in children. Flexible instruments are primarily useful (in children) for diagnostic purposes, since they are generally unsuitable for extraction of foreign bodies and other operative procedures; rigid instruments are superior for such applications. Particular advantages of flexible bronchoscopes include their ability to pass through endotracheal or tracheostomy tubes, the fact that they produce little anatomic distortion of the airway structures or dynamics, and their ease of use in sedated, spontaneously breathing patients.

The standard pediatric flexible bronchoscope has a 3.5- to 3.7-mm outside diameter and a 1.2-mm suction channel. This instrument can be used in infants as small as 700 g, and most term newborns can breathe around it spontaneously, at least for short periods.[8] However, the smallest endotracheal tube through which this bronchoscope can pass is 4.5 mm in inner diameter. Therefore, the examination of the lower airways in intubated infants usually requires extubation, use of a rigid bronchoscope, or use of a smaller flexible bronchoscope. "Ultrathin" flexible bronchoscopes are now available that will pass through endotracheal tubes as small as 2.5 mm in inner diameter. These instruments have limited but important applications.[3-10]

We have used these ultrathin instruments for the past several years and have found them to be indispensable adjuncts to rigid and standard pediatric flexible bronchoscopes. Their small size permits relatively unusual applications. We present here four illustrative case reports.

INSTRUMENTATION

The flexible bronchoscopes used in this report were obtained from the Olympus Corporation of America (Lake Success, NY). The standard, 3.5-mm pediatric flexible instrument was the BF3C10. Two different ultrathin instruments were employed. The PF27M is 2.7 mm in outer diameter, and the BF22 is 2.2 mm in outer diameter. Both instruments lack a suction channel, but the tip can be flexed 180° up and 60° down. When the bronchoscopes were passed through endotracheal or tracheostomy tubes during mechanical ventilation, a bronchoscopic swivel adapter (Portex, Inc, Wilmington, Mass) was used with a customized diaphragm to fit the ultrathin bronchoscope.

CASE REPORTS

Case 1. The patient was referred at 4 months of age for persistent stridor and wheezing unresponsive to therapy. Diagnostic flexible bronchoscopy revealed the presence of complete tracheal rings beginning at the thoracic inlet. The diameter of the stenotic region of the trachea was smaller than that of the 3.5-mm flexible bronchoscope. An ultrathin instrument (BF22) was therefore used to examine the lower trachea and bronchi. The patient could not ventilate while the 2.2-mm bronchoscope passed through the stenotic region, so the bronchoscope was intermittently withdrawn into the upper trachea. The complete cartilage rings were found to extend to the second ring above the carina. The right upper lobe bronchus arose from the distal trachea; the remainder of the bronchial anatomy was normal.

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The length of the stenotic tracheal segment was such that resection with end-to-end anastomosis was not feasible. Through a median sternotomy incision, the trachea was exposed and opened longitudinally. Two 18-gauge vascular catheters were passed through the endotracheal tube and manually introduced into each main stem bronchus. These catheters were used for jet ventilation[11] until the tracheal repair was completed. The tip of the endotracheal tube (3.5 mm inner diameter) was positioned just at the carina, and a costal cartilage graft was sutured into position in the ventral aspect of the trachea with use of the endotracheal tube as a stent. The 2.2-mm flexible bronchoscope was passed through the endotracheal tube to examine the distal suture line. Despite the presence of the jet ventilation catheters and the bronchoscope, adequate ventilation was maintained, and a good view of the anastomosis was obtained. We were thus able to inspect the luminal aspect of the repair intraoperatively without interrupting ventilation, extubating the patient, or disturbing the graft. The ultrathin bronchoscope was used repeatedly during the postoperative period to evaluate the status of the tracheal repair. Initially, this evaluation was performed via the endotracheal tube (which was left in position as a stent for 10 days). After extubation, several bronchoscopic examinations were required to assess airway patency. The ultrathin instrument was also used for these examinations, because it resulted in minimal increase in airway resistance. The patient has done well during 26 months of follow-up.

Case 2. A 6-month-old boy with severe tracheomalacia associated with a previously corrected esophageal atresia and tracheoesophageal fistula underwent emergency laparotomy for intestinal obstruction. He remained intubated in the postoperative period and after 3 days developed severe respiratory distress. The lower trachea was examined with an ultrathin flexible bronchoscope passed through the endotracheal tube, revealing total obstruction of the trachea by an accretion of crusted mucus. The bronchoscope could not be pushed through or past this obstruction. The endotracheal tube was therefore forcibly advanced past the obstruction and into the right main bronchus. This relieved the obstruction and the patient was successfully resuscitated. After extensive lavage with saline and 1% *N*-acetyl-L-cysteine and suctioning, reexamination disclosed virtually total loss of the tracheal mucosa and nearly total collapse of the trachea in the lower third of its length. Apparently, routine suctioning had denuded the trachea. It was also obvious that correction of the underlying structural lesion would be necessary. The endotracheal tube was positioned with its tip just above the carina (position documented with the bronchoscope), and the patient was taken to the operating room.

A median sternotomy was performed and the adventitia of the aortic arch, innominate artery, and anterior tracheal wall was suspended from the posterior aspect of the sternum with sutures. Just prior to closure of the sternum and placement of the final knots in the suspension sutures, the tracheal lumen was inspected with the ultrathin bronchoscope through the endotracheal tube. By partially withdrawing the endotracheal tube we were able to view the distal trachea without interrupting ventilation. Hence, we were able to adjust the suspension sutures to achieve a satisfactory tracheal lumen without excessive tension. The airway was inspected again after the procedure was completed to verify the success of the aortopexy. The patient did well in the postoperative period but died several months later of unrelated sepsis.

Case 3. The patient was a 14-month-old boy with cerebrocostomandibular syndrome[12] who had undergone tracheostomy at 3 weeks of age. Because of complete airway obstruction when the tracheostomy tube was removed, his airway was inspected with a flexible bronchoscope. Granulation tissue was found to completely occlude the trachea above the tracheostomy stoma. An attempt to remove the granulation tissue with a rigid bronchoscope failed because of the very small mandible and extreme anterior position of the larynx. Therefore, the patient was intubated transnasally by means of an ultrathin flexible bronchoscope to guide the 4.0-mm endotracheal tube. The tube could be passed beyond the granulation tissue when the tracheostomy tube was removed, and the patient was ventilated through the tube, around the bronchoscope. The tip of the endotracheal tube was withdrawn to just above the granulation tissue, and the view of the airway was displayed on a video monitor. Under this indirect visualization, instruments were passed through the tracheostomy stoma to grasp and remove the granulation tissue. The endotracheal tube was intermittently passed beyond the obstruction for ventilation as needed. Following removal of the granulation tissue, the tracheostomy tube was replaced and the patency of the suprastomal trachea was verified visually through the bronchoscope. The postoperative course was uneventful.

Case 4. A 2-year-old girl suffered severe midfacial injuries in a motor vehicle accident. A tracheostomy was performed to facilitate mechanical ventilation. Approximately 8 hours later, severe respiratory distress with acidosis, very high peak airway pressures, and increased intracranial pressure led us to examine her lower airways through the tracheostomy tube, using an ultrathin flexible bronchoscope. At that time her arterial pH was 6.94, P_{CO_2} was 104, and P_{O_2} was 221 on 100% oxygen. The trachea and both main bronchi were found to be filled with a dried, tenacious mixture of aspirated blood and mucus (analogous to a saddle embolus) that could not be removed with suction catheters.

Because of an unstable cervical spine, a rigid bronchoscope could not be safely inserted through either the mouth or the tracheostomy stoma.

The patient was then intubated orally with a 4.5-mm endotracheal tube by means of a 3.5-mm flexible bronchoscope to guide the tube. This intubation was facilitated by the ability to suction blood and secretions through the bronchoscope. The tip of the tube was positioned just above the tracheostomy tube, and the 3.5-mm bronchoscope was replaced with an ultrathin (2.2 mm) bronchoscope. The tracheostomy tube was removed and ventilation was maintained through the endotracheal tube. Various instruments were passed through the tracheostomy stoma, with guidance by direct visualization through the bronchoscope, to grasp and remove the blood-mucus plug filling the trachea and both main stem bronchi. (Blind attempts failed.) The 3.5-mm flexible bronchoscope was then passed through the stoma to lavage and extensively suction and clean the main stem, lobar, and segmental bronchi of residual mucus and blood. The tracheostomy tube was then replaced. By the end of the procedure, the arterial pH had risen to 7.16, the P_{CO_2} had fallen to 58 (7.38 and 29, 1 hour later), and the intracranial pressure had normalized. The child subsequently developed severe adult respiratory distress syndrome, recovered, and was successfully decannulated. She is well on follow-up 1 year later.

DISCUSSION

Ultrathin flexible bronchoscopes offer many possibilities for examination of the lower airways of infants and small children. The most important of these is the ability to pass through small endotracheal or tracheostomy tubes while maintaining effective gas exchange. The BF22 can pass through a 2.5-mm endotracheal tube, and with an endotracheal tube as small as 3 mm or a size 00 tracheostomy tube, the patient can be ventilated with the instrument in place. The standard pediatric flexible bronchoscope, 3.5 mm in diameter, can pass through a 4.5-mm endotracheal tube, but the minimal tube size that will allow ventilation is 5.5 mm.

In three of the four patients reported here, the ultrathin bronchoscope made a unique contribution to diagnosis, providing information that would otherwise have been extremely difficult if not impossible to obtain under the circumstances. In cases 2 and 4, this diagnostic information was immediately lifesaving. Although lower airway obstruction was clinically apparent, suctioning or even changing the endotracheal or tracheostomy tubes would have been ineffective, and only the endoscopic examination led to the correct action.

The ability to visualize the lower airways through small-caliber endotracheal tubes while maintaining ventilation, and to thereby direct operative manipulation, is potentially very important. In cases 1 and 2, it was critical to the success of the intrathoracic operative procedure that the endotracheal tube not be disturbed, and for the neck not to be extended during the observation. Although in theory the lower airways could have been examined with a rigid telescope or even a 3.5-mm flexible bronchoscope, extubation and reintubation would have been required. In case 1 this action would have risked dislodgment of the cartilage graft, while in case 2 it would have been very difficult to evaluate the tension on the tracheal wall prior to closure of the sternal incision. Thus, only the ultrathin instrument was appropriate to the situation. In cases 3 and 4, the ultrathin bronchoscope was used to guide instruments passed through the tracheostomy stoma to remove tissue or other material obstructing the airway. In both patients, the use of rigid bronchoscopes was not feasible — in one case because of cervical instability and in the other because of extreme mandibular hypoplasia.

In elective circumstances, the use of a video camera and monitor to display the endoscopic view to all personnel involved with the patient can be helpful. In two of our patients, because of the emergency nature of their problems, our video equipment was not brought to the intensive care unit and only a teaching attachment was used. It is important to have this capability so that at least one other individual may observe simultaneously with the bronchoscopist.

We have used the ultrathin bronchoscopes for other purposes as well, including the in situ evaluation of the placement of tracheostomy tubes and the dynamics of the posterior trachea near the tip of tracheostomy tubes, and for retrograde direct laryngoscopy in infants with tracheostomies. We have also used the instruments to direct the placement of Gruentzig balloon catheters for dilation of bronchial stenoses in infants,[13,14] to examine peripheral airways beyond the fifth generation in infants, and for the intraoperative assessment of bronchial patency during pulmonary resection in infants. Ultrathin flexible bronchoscopes with distal flexion capability are extremely useful for difficult intubations in small infants.[3,10]

While the ultrathin flexible instruments are designed and marketed as bronchoscopes, they obviously have applications far beyond the lower respiratory tract. Their small diameter allows exploration of many other orifices such as the eustachian tubes and ureters. The lack of a suction channel is potentially a problem, since secretions cannot be aspirated and the lens may become obscured. Nevertheless, these instruments have clear potential for very important applications in both diagnostic and therapeutic situations, especially in small infants.

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AMERICAN CLEFT PALATE–CRANIOFACIAL ASSOCIATION

The 48th Annual Meeting of the American Cleft Palate–Craniofacial Association will be held March 18-21, 1991, at the Hyatt Regency Hotel in Hilton Head, South Carolina. The Association is composed of 2,500 members from nearly 40 countries who are dedicated to improving the quality of life for persons with cleft lip and cleft palate and related craniofacial anomalies. For further information, contact Nancy C. Smythe, American Cleft Palate–Craniofacial Association, 1218 Grandview Avenue, Pittsburgh, PA 15211; (412) 481-1376, FAX (412) 481-0847.

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STAPES SURGERY IN OSTEOGENESIS IMPERFECTA: ANALYSIS OF POSTOPERATIVE HEARING LOSS

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The disappointing results in 12 of 58 stapedectomies, including 4 revision operations, performed on osteogenesis imperfecta patients were analyzed and compared with reports in the literature. It is concluded that the results described as disappointing were not always the product of the stapes operation. A progressive sensorineural hearing loss arising independently of the operation as a result of progression in the disease process of osteogenesis imperfecta appears to have a severe influence on the final hearing threshold.

KEY WORDS — deafness, genetic deafness, hearing loss, osteogenesis imperfecta, stapes ankylosis, stapes surgery.

INTRODUCTION

Osteogenesis imperfecta is characterized by brittleness of the bones, blue sclerae, and progressive hearing loss. The hearing loss usually begins in the second or third decade. It can be a pure conductive or a mixed loss. Pure perceptive losses, especially of the higher frequencies, are common.[1] The conductive component in the hearing loss is usually the result of fixation of the stapes footplate, as in otosclerosis; sometimes there is a stapes fracture. Until the 1970s, the middle ear changes in osteogenesis imperfecta were considered to be a severe form of otosclerosis.[2-4] Stapes surgery in osteogenesis imperfecta was therefore considered to be risky.[5] On histologic, biochemical, and clinical-genetic grounds, it must be recognized that otosclerosis and osteogenesis imperfecta are not only different disease entities,[6-16] but also that osteogenesis imperfecta represents a group of various different disease processes that sometimes have very similar clinical manifestations.[17-20]

To improve the hearing loss, fenestration of the lateral semicircular canal was performed in the 1940s and 1950s,[2,21-25] followed later by stapes mobilization.[23,25,26] These operations had little success. The first successful report of stapedectomy in osteogenesis imperfecta appeared in 1960.[23] More publications followed later, usually covering a small number of operations with variable success.[5,25,27-37] It was not until the 1980s that a few series were published that reported on ear operations in more than 10 patients. The results were usually good.[38-42] The operative findings and the short-term and long-term results of stapes surgery are reported, especially in the three largest studies.[39,40,42]

This article presents an analysis of the disappointing results among the 58 ears in the Dutch series of stapes operations for osteogenesis imperfecta. A review of the relevant literature is also given.

PATIENTS AND METHODS

We studied hearing loss in sufferers of osteogenesis imperfecta by collecting data on stapes surgery in this disease. We combined data from the Nijmegen series[37,41] with those from other Dutch otologic surgeons. Some of these cases were reported spontaneously by these otologic surgeons following an appeal for such cases, while others were traced through a study of hearing loss in Dutch patients with osteogenesis imperfecta. The Dutch Association of Patients with Osteogenesis Imperfecta also lent its active support. A retrospective study of the operation reports was therefore made, and where possible, all audiologic data were traced. At the same time, an attempt was made to extend the follow-up period by performing new pure tone audiometry studies. Other, nonotologic data such as the number of fractures were also collected.[42] This Dutch series contained 58 stapedectomies in 47 patients with osteogenesis imperfecta. They were operated on during the period from 1960 to 1988 for fixation of the stapes. In 4 of the 58 ears, a revision operation was also performed.

In 12 of the 58 stapes operations, the ultimate re-

TABLE 1. SEX DISTRIBUTION OF PATIENTS

	Shea and Postma[39]	*Pedersen and Elbrond*[40]	*Others*[5,25,29-35,38]	*This Series*[41,42]	*Total*	*Presumed Failures*
Men (No.)	14	13	11	17	55	3
Women (No.)	29	19	41	30	119	7
Unknown (No. of patients)	—	—	4	—	4	—
M:F ratio	1:2.1	1:1.5	1:3.7	1:1.8	1:2.2	1:2.3

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TABLE 2. NUMBER OF FRACTURES

	Shea and Postma[39]		*Pedersen and Elbrond*[40]		*Others*[5,25,29-35,38]		*This Series*[41,42]		*Presumed Failures*	
No. of Fractures	*No. of Pts*	*%*	*No. of Pts*	*%*	*No. of Pts*	*%*	*No. of Pts*	*%*	*No. of Pts*	*%*
<3	17	40	—	—	4	7	5	11	2	20
3 or more	26	60	—	—	14	25	40	85	7	70
Unknown	0	0	—	—	38	68	2	4	1	10
0	—	—	0	0	—	—	1	2	0	0
1-5	—	—	6	19	—	—	14	30	3	30
6-9	—	—	5	17	—	—	3	6	0	0
10-29	—	—	15	47	—	—	19	40	5	50
30 or more	—	—	4	13	—	—	8	17	1	10
Unknown	—	—	2	6	—	—	2	4	1	10
Total	43		32		56		47		10/47	

Dash — not applicable for lack of data.

sults proved disappointing, either directly after the operation and within a period of 12 months, or after more than 12 months. These operations were in 10 patients — 3 men and 7 women ranging in age from 15 to 45 years — who underwent stapes surgery between 1963 and 1988.

In order to be considered as disappointing, a result had to meet the following criteria:

1. Directly after the operation: an increase in the hearing loss, failure to achieve a hearing gain of more than 10 dB Fletcher-index (mean hearing loss at 0.5, 1, and 2 kHz), or an increase of the bone conduction threshold of 10 dB Fletcher-index or more despite an improvement in the air conduction threshold of more than 10 dB Fletcher-index.
2. After 12 months postoperatively: an increase in the air conduction threshold of more than 20 dB Fletcher-index, or an increase of the bone conduction threshold of an average of 15 dB or more Fletcher-index.

We looked for common factors in these disappointing results (presumed failures) as compared with the successful operations. Features such as age at onset of hearing loss, the age at which the first stapes operation took place, the number of fractures, the sex of the patient, the technique of stapes surgery, the perioperative findings, and the preoperative bone conduction thresholds, from our complete group of 58 ears and from comparable studies,[5,25,29-35,38-40] were compared retrospectively in order to see if there are indicators of a reduced chance of a successful operation.

RESULTS

Data could be gathered from 47 patients who had undergone operations in the Netherlands for stapes fixation during the period from 1960 to 1988. There were 17 men and 30 women; the sex ratio was therefore 1 to 1.8. Table 1[5,25,29-35,38-42] also presents the sex ratio for the patient groups of an American study,[39] a Danish study,[40] and a combination of 10 studies compiled by us.[5,25,29-35,38] The data from the 12 of 58 ears in which the results could be described as disappointing are listed separately (presumed failures).

Of 174 out of 178 patients who underwent ear operations, there are 119 women (68%) and 55 men (32%). Table 2[5,25,29-35,38-42] notes the number of fractures for our patients as well as for those of other series. The age (by decade) at which the first stapes operation was performed is stated for each patient in Table 3.[5,25,29-35,38-42] The ages in the

TABLE 3. AGE AT TIME OF FIRST STAPES OPERATION

	Shea and Postma[39]		*Pedersen and Elbrond*[40]		*Others*[5,25,29-35,38]		*This Series*[41,42]		*Total*		*Presumed Failures*	
Age (y)	*No. of Pts*	*%*	*No. of Pts*	*%*	*No. of Pts**	*%*	*No. of Pts*	*%*	*No. of Pts*	*%*	*No. of Pts*	*%*
0-9	—	—	0	0	1	3	0	0	1	1	0	0
10-19	—	—	4	13	6	21	7	15	17	16	2	20
20-29	—	—	14	44	7	24	18	38	39	36	4	40
30-39	—	—	7	22	4	14	11	23	22	20	3	30
40-49	—	—	4	13	9	31	8	17	21	19	1	10
50-59	—	—	3	9	1	3	2	4	6	6	0	0
60 or more	—	—	0	0	1	3	1	2	2	2	0	0
Total	—		32		29		47		108		10/47	
Mean age	—		31.0		32.3		30.6		31.2		27.6	
Range (y)	—		—		9-66		10-63		9-66		15-44	

Dash — not applicable for lack of data.
*Data unknown for 27 patients.

TABLE 4. AGE AT ONSET OF HEARING LOSS

	Shea and Postma[39]		*Pedersen and Elbrond*[40]		*Others*[5,25,29-35,38]		*This Series*[41,42]		*Total*		*Presumed Failures*	
Age (y)	*No. of Pts*	*%*	*No. of Pts*	*%*	*No. of Pts*	*%*	*No. of Pts*	*%*	*No. of Pts*	*%*	*No. of Pts*	*%*
0-9	2	5	2	6	1	2	10	21	15	9	3	30
10-19	18	44	11	34	4	7	16	34	49	28	5	50
20-29	8	20	11	34	6	11	11	23	36	20	1	10
30-39	5	12	6	19	2	4	4	9	17	10	1	10
40-49	5	12	2	6	0	0	2	4	9	5	0	0
50 or more	3	7	0	0	0	0	0	0	3	2	0	0
Unknown	0	0	0	0	43	77	4	9	47	27	0	0
Total	41		32		56		47		176		10/47	

Dutch series range from 10 to 63 years, with an average of 30.6 years. For the 12 ears in which results were considered disappointing, the age at operation was even lower. For the 6 of these 12 ears in which there was an increase in hearing loss directly after the operation, the average age at stapes surgery was 20.0 years, as opposed to 36.3 years for the 6 ears with hearing loss that occurred later. Table 4[5,25,29-35,38-42] and Table 5[5,25,29-35,38-42] show that 26 of the 43 patients (60%) already had hearing loss before 20 years of age and that the average age at onset was 18.4 years. In the group with disappointing results, this was the case in 8 of 10 patients (80%), with an average age at onset of hearing loss of 16.6 years. On average, the age at onset of hearing loss in the Danish, American, and combined groups ("Others") was several years later.

The various techniques for performing stapes surgery, as well as those for total stapedectomy, partial platinectomy, stapedotomy, and partial stapedectomy are listed in Table 6[5,25,29-35,38-42] and Table 7.[5,25,29-35,38-42] In 31 of 58 ears (53%) a total stapedectomy was performed, but after 1980, partial platinectomy and stapedotomy were more frequently performed. Before 1980, only 4 of 27 ears (15%) were treated by partial platinectomy or stapedotomy; after 1980, 22 of 31 ears were (71%).

The operative findings in the stapes footplate, the stapes crura, and the middle ear mucosa in the region of the oval window are listed in Table 8.[5,25,29-35,38-42] A moderate-to-severe thickening of the footplate was found in 32 of 58 ears (55%). In all the studies together, this was found in 134 of 234 ears (57%). In the group with disappointing results, the footplate was thickened in 10 of the 12 ears (83%). Further differentiation showed that the majority of the thickened footplates were solidly thickened — a finding sometimes observed in the form of an obliteration of the oval window. In the present study, this finding was seen in 22 of the 32 thickened footplates (69%). In the group with disappointing results and in the study of Shea and Postma,[39] all thickening of the footplate was solid. In 15 of the 58 ears (26%) in the present study a soft or friable footplate consistency was reported, and in all the studies together, this was found in 61 of 234 ears (26%). The group with disappointing results shows no differences here. Thickened edges and/or bony apposition anteriorly and posteriorly on the footplate, which hinders a good approach, was seen in 11 of the 58 ears (19%). In all studies together this was seen in 25 of 234 ears (10% [.098]). In the group with disappointing results, it was found in 4 of 12 ears (33%). A remarkable number of reports in the present study state that even the footplate itself bled easily during the operation (8 of 58 ears or 14%). In all studies together this was reported in 9 of 234 ears (4%), and in the group with disappointing results, in 3 of 12 ears (25%). The presence of a floating footplate is sometimes correlated to a thick and soft footplate. If it should be necessary to remove the stapes superstructure early, without being able to introduce a safety hole into the footplate, the chance of a floating footplate will clearly be increased, partly because of the reduced fixation. This occurrence was seen in 2 of the 12 ears (17%) with disappointing results. In all studies together, a floating footplate occurred in 5 of 234 ears (2%), with a resultant increase in sensorineural hearing loss.[30,32,42]

In 11 of 58 ears (19%), detailed information about the configuration of the stapes crura was not available. Normal crura were found in 112 out of 234 ears (48%), although there was some variation among the individual studies. In 10 of 58 ears (17%) the crura appeared to be interrupted. This

TABLE 5. MEAN AGE AT ONSET OF HEARING LOSS

	Shea and Postma[39]	*Pedersen and Elbrond*[40]	*Others*[5,25,29-35,38]	*This Series*[41,42]	*Total*	*Presumed Failures*
No. of patients	—	32	37	43	112	10/47
Unknown	—	0	19	4	23	0
Mean age at onset	—	23.0	22.4	18.4	21.0	16.6
Range	—	—	9-36	5-46	5-46	8-32

Dash — not applicable for lack of data.

TABLE 6. METHODS OF STAPES SURGERY

	Shea and Postma[39]		*Pedersen and Elbrond*[40]		*Others*[5,25,29-35,38]		*This Series*[41,42]		*Presumed Failures*	
Methods of Surgery	*No. of Ears*	*%*	*No. of Ears*	*%*	*No. of Ears*	*%*	*No. of Ears*	*%*	*No. of Ears*	*%*
Fat/vein/Gelfoam-wire	—	—	22	51	25	35	6	10	2	17
Teflon-piston	—	—	7	16	1	1	20	35	6	50
Teflon-wire	—	—	0	0	6	8	20	35	3	25
Teflon-cup/loop	—	—	0	0	0	0	6	10	0	0
Vein-polyethylene strut	—	—	11	26	1	1	4	7	1	8
Malleus-handle piston	—	—	0	0	0	0	1	2	0	0
Autologue interposition										
Stapedioplasty	—	—	1	2	0	0	0	0	0	0
Portmann type II	—	—	0	0	0	0	1	2	0	0
Unknown	62	100	2	5	38	54	0	0	0	0
Total	62		43		71		58		12/58	

Dash — not applicable for lack of data.

finding was reported in 29 of the 234 ears (12%), with an individual variation of 0% to 20%. The crura were thin and/or atrophic in 22 of the 58 ears (38%). A total of 67 of the 234 ears (29%) had similar crura. In the group with disappointing results, thin and/or atrophic crura were found in 5 of 12 ears (42%), and there were no fractures.

A thickened mucosa was seen in 7 of the 58 ears (12%) and in 22 of the 234 ears (9%), with individual variations of between 0% and 28%. In the group with disappointing results, however, a thickened mucosa was found in 5 of the 12 ears (42%). It is also remarkable that in 12 of the 58 ears (21%) it was stressed that the mucosa bled readily, while in 19 ears (33%), there is no report of this; and the mucosa was described as normal in 24 of the 58 ears (41%). In all studies together, a remarkably hemorrhagic mucosa was reported in 49 of the 234 ears (21%). This abnormality, too, occurs more frequently in the group with disappointing results (5 of 12 ears or 42%).

In total, we established that for 12 of these 58 stapes operations (21%), the results directly after the operation or after a period of more than 12 months were disappointing according to our standards. The preoperative and postoperative hearing levels of these 12 ears in 10 patients are presented in Figs 1-7, together with the simultaneously recorded hearing levels in the 8 contralateral ears. Table 9 reports the ear, sex, and age of each of these 10 patients, as well as the findings during operation, the type of piston used, the complications noted during operation as documented in the surgical report, and some other special findings. An increase in hearing loss compared with the preoperative hearing threshold was noted directly after the operation in 5 of the 12 ears (42%) (Figs 1-3; patients 1 right, 2, 3, 4, and 5). The hearing threshold was unchanged directly after the operation in 1 of the 12 ears (8%) (Fig 1; patient 1 left). An acceptable-to-good hearing gain was achieved in 5 of the 12 ears (42%) (Figs 4-6; patients 6 both, 7, 8, and 9). One of the 12 ears (8%) has been included in the totals although data are not available that could demonstrate any relationship between the operation and the hearing result (Fig 7; patient 10). It is remarkable that despite the findings and the events (Table 9), no ear became completely deaf after operation, although 3 of the 12 ears (patients 1 left and 6 both) developed a hearing loss of more than 90 dB at a later stage. In the other studies[5,25,29-35,39,40] complete deafness arose in 5 of 176 ears (3%) (Table 10[29,30,32,39]; patients 11-15). In 1 of the 5 ears (patient 12) the deafness arose only after 3 years, as opposed to the other 4 ears, in which a direct relationship with the operation could be established. In order to investigate if the size of the sensorineural component of the preoperative hearing loss could influence the chances of an unfavorable postoperative result, we collated the preoperative bone conduction thresholds and their averages from the various studies (Table 11[5,25,29-35,38-42]). It is remarkable that in the present study, in the group with disappointing results, and in the study of Shea and Postma[39] the several sensorineural hearing thresholds are

TABLE 7. TYPES OF STAPES SURGERY

	Shea and Postma[39]		*Pedersen and Elbrond*[40]		*Others*[5,25,29-35,38]		*This Series*[41,42]		*Presumed Failures*	
Types of Surgery	*No. of Ears*	*%*	*No. of Ears*	*%*	*No. of Ears*	*%*	*No. of Ears*	*%*	*No. of Ears*	*%*
Total stapedectomy	62	100	37	86	39	55	31	53	10	83
Partial platinectomy	0	0	1	2	1	1	12	21	0	0
Stapedotomy	0	0	2	5	0	0	14	24	2	17
Partial stapedectomy	0	0	1	2	1	1	1	2	0	0
Unknown	0	0	2	5	30	42	0	0	0	0
Total	62		43		71		58		12/58	

TABLE 8. FINDINGS DURING STAPES OPERATION

Findings at Operation	*Shea and Postma*[39] *No. of Ears*	*%*	*Pedersen and Elbrond*[40] *No. of Ears*	*%*	*Others*[5,25,29-35,38] *No. of Ears*	*%*	*This Series*[41,42] *No. of Ears*	*%*	*Presumed Failures* *No. of Ears*	*%*
Footplate										
Fixed	62	100	43	100	70	99	54	93	11	92
Thick	31	50	23	53	48	68	32	55	10	83
Slightly	0	0	0	0	0	0	0	0	0	0
Moderately	0	0	0	0	0	0	10	17	0	0
Solid	31	50	0	0	0	0	22	38	10	83
Soft	4	6	6	14	36	51	15	26	2	17
Bleeding	0	0	0	0	1	1	8	14	3	25
Thick rims	14	23	0	0	0	0	11	19	4	33
Unknown	0	0	0	0	1	1	4	7	1	8
Stapes crura										
Fractured	0	0	5	12	14	20	10	17	0	0
Thin/atrophic	13	21	14	33	18	25	22	38	5	42
Brittle	0	0	11	26	0	0	0	0	0	0
Normal	49	79	12	28	32	45	19	33	4	33
Unknown	0	0	6	14	9	13	11	19	3	25
Mucosa										
Thick	0	0	12	28	3	4	7	12	5	42
Bleeding	18	29	13	30	6	8	12	21	5	42
Normal	44	71	21	49	8	11	24	41	3	25
Unknown	0	0	5	12	54	76	19	33	3	25
Total ears	62		43		71		58		12/58	

equally divided. In the study of Pedersen and Elbrond[40] and the combined studies,[5,25,29-35] it is principally the lowest perception thresholds that are present in the largest percentage. The averages of the preoperative bone conduction thresholds are clearly higher in the present study than in the other studies.

In the present study revision operations were performed in a total of 4 out of 58 ears (7%). In 2, the long process of the incus proved to be eroded, in 1 case there were also remnants of a chronic otitis media, and in 1, the revision was performed following considerable external trauma. Only in 1 case did the revision result in a slight improvement in hearing

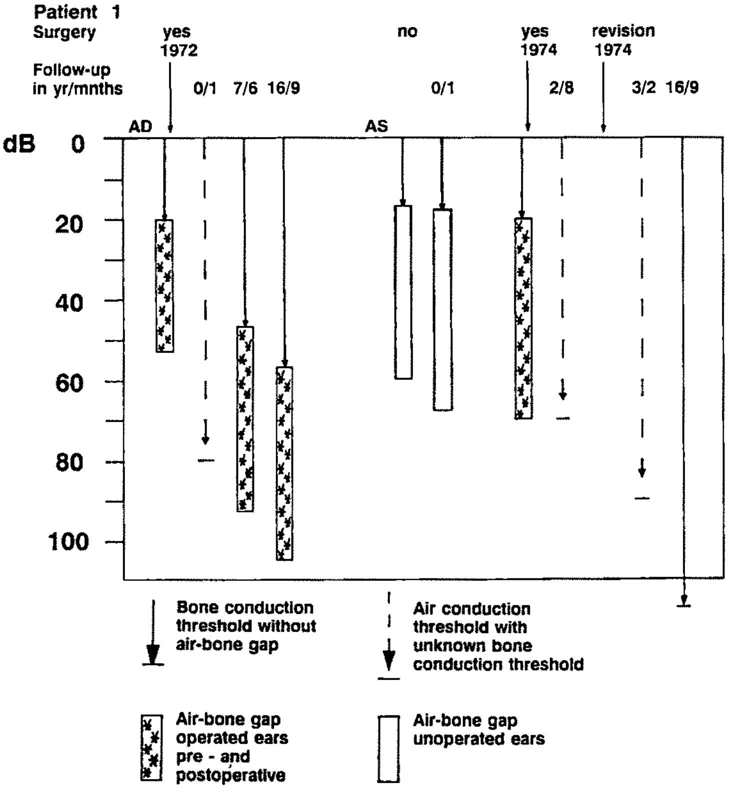

Fig 1. (Patient 1) Follow-up results in terms of average pure tone thresholds (decibels hearing level) for frequencies 500, 1,000, and 2,000 Hz.

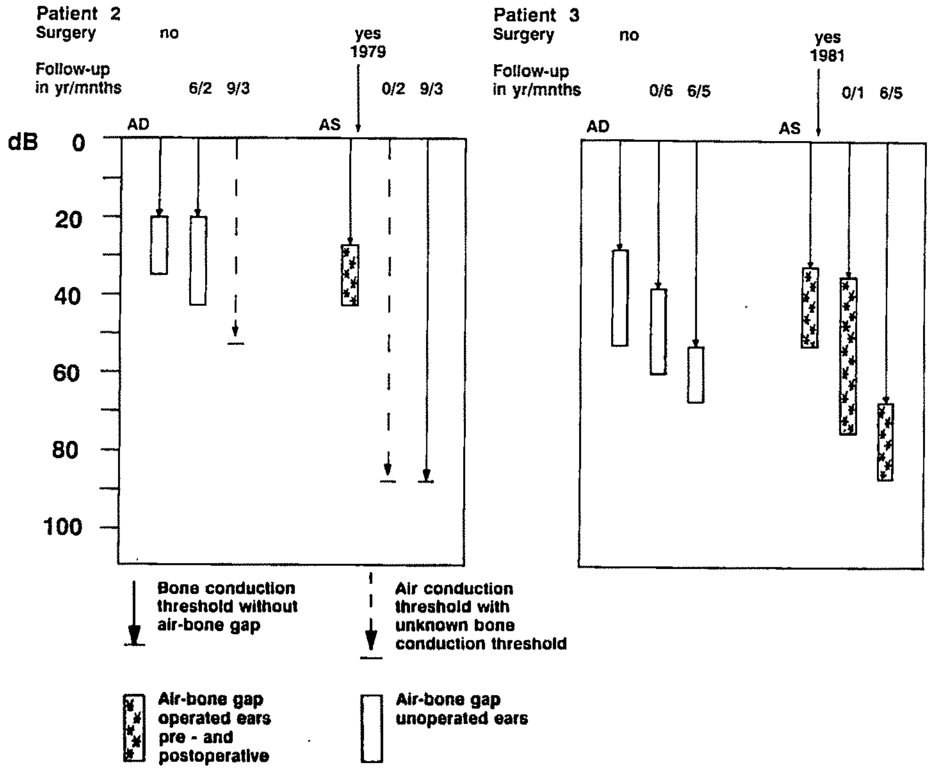

Fig 2. (Patients 2 and 3) Follow-up results in terms of average pure tone thresholds (decibels hearing level) for frequencies 500, 1,000, and 2,000 Hz.

(Fig 3; patient 4). In the other 3, a hearing loss resulted, most probably completely sensorineural in nature (Figs 1, 5, and 6; patients 1 left, 8, and 9).

In the other studies, revision took place in 15 of 176 ears (9%). The findings in 5 of these 15 revisions are known (Table 12[25,29,34]; patients 16-19). From the total of 9 revisions described, adhesions and granuloma formation were present in 3 of them. In 1 ear, the oval window was obliterated. In 3 ears, the incus was eroded, and in 1 case the strut was too short — a finding that could also indicate erosion. In 1 case trauma had loosened the piston.

Of the 19 revisions from all the studies, only 6

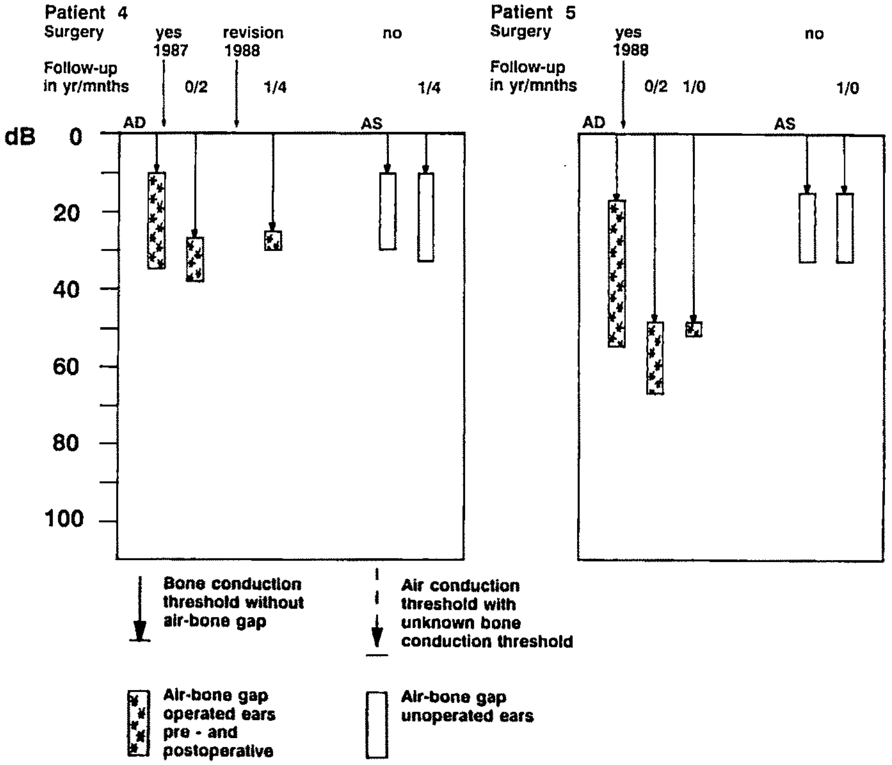

Fig 3. (Patients 4 and 5) Follow-up results in terms of average pure tone thresholds (decibels hearing level) for frequencies 500, 1,000, and 2,000 Hz.

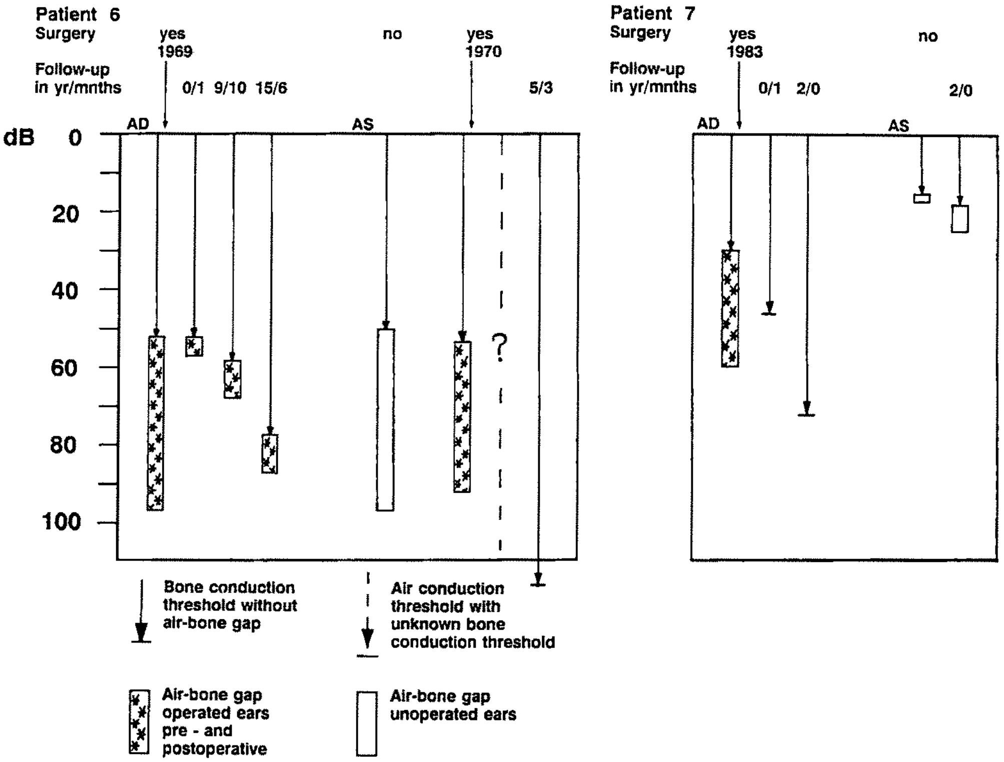

Fig 4. (Patients 6 and 7) Follow-up results in terms of average pure tone thresholds (decibels hearing level) for frequencies 500, 1,000, and 2,000 Hz.

(32%) showed an adequate-to-good result or closure of the air-bone gap. In 5 ears there was deterioration of hearing and in 1 case it was unchanged. The data for 3 ears are unavailable. In 4 ears, deafness resulted that was as good as total.

DISCUSSION

It is probable that the clinical presentation and also the nature of the hearing loss in osteogenesis imperfecta are the same as in otosclerosis. The dis-

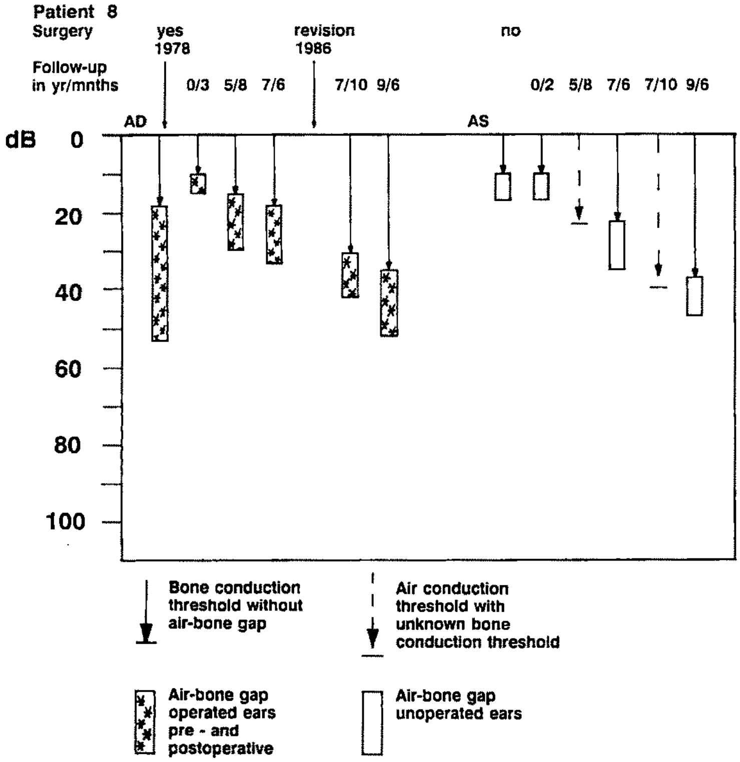

Fig 5. (Patient 8) Follow-up results in terms of average pure tone thresholds (decibels hearing level) for frequencies 500, 1,000, and 2,000 Hz.

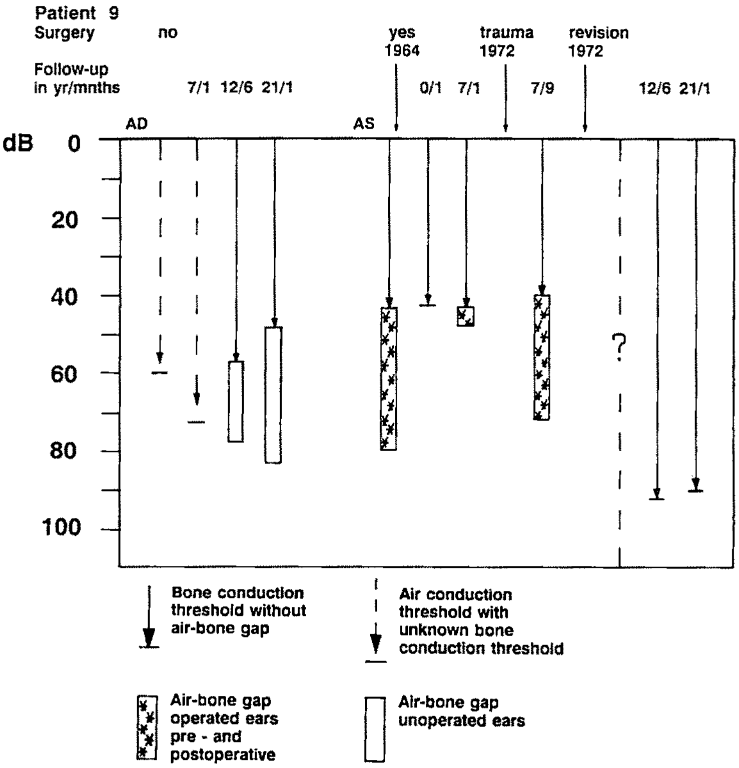

Fig 6. (Patient 9) Follow-up results in terms of average pure tone thresholds (decibels hearing level) for frequencies 500, 1,000, and 2,000 Hz.

tribution with regard to sex shows a female predominance of at least 2 to 1 in the 174 operated cases of osteogenesis imperfecta. The figures known from operated cases of otosclerosis patients are almost exactly the same.[8,43,44] The onset of hearing loss before the 20th year was established in a total of 64 of 129 patients (50%) (Table 4), without a descriptive definition of this level of hearing loss being given. Otosclerosis also presents at a very young age, but less frequently so than osteogenesis imperfecta. Robinson[45] found an onset of hearing loss before the age of 18 years in 610 of 4,014 otosclerosis patients (15%). In our group with disappointing results, 8 of the 10 patients (80%) were hard of hearing before 20 years of age. The question arises as to whether patients with an increased risk can be recognized in advance. First of all, it appears that these patients already have considerable loss of hearing at an early age (Tables 4 and 5), and generally, they come to operation at a younger age (4.5 years younger) than average (Table 3). In the group with an increase in hearing loss directly after the operation, the average age at stapes surgery is even as low as 20.0 years, as opposed to 36.3 years in the group with hearing loss in the long term. Furthermore, the at-risk patient has a solidly thickened footplate (83%) with thickened edges (33%) and hemorrhage (25%) (Table 8). The crura are thin and atrophic (42%). The mucosa of the middle ear is thicker than normal (42%) and also leads to troublesome hemorrhage (42%). It also appears that the at-risk patient has a higher preoperative bone conduction threshold (Table 11). On the other hand, the at-risk patient shows no differences with regard to sex (Table 1), the number of fractures (Table 2), or the materials used during the stapes operation (Table 6). However, a total stapedectomy had usually been performed in the group with disappointing results

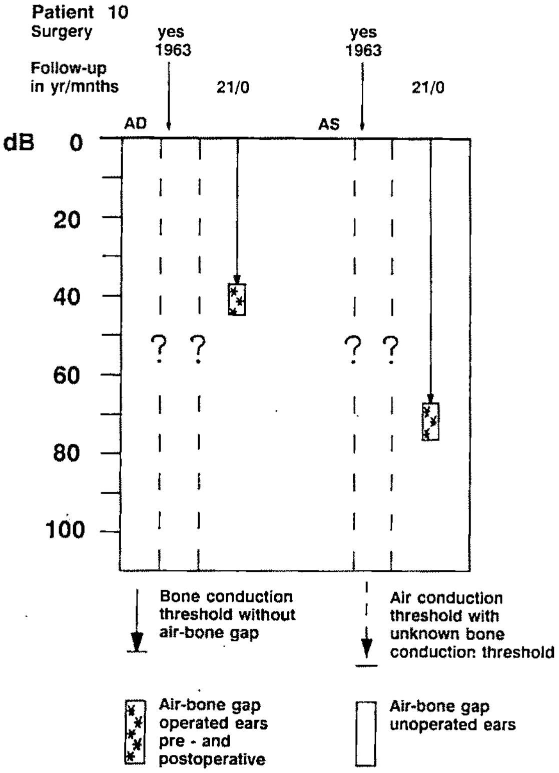

Fig 7. (Patient 10) Follow-up results in terms of average pure tone thresholds (decibels hearing level) for frequencies 500, 1,000, and 2,000 Hz.

TABLE 9. FINDINGS AT 12 STAPEDECTOMIES IN 10 PATIENTS WITH DISAPPOINTING RESULTS

Pt	*Sex*	*Ear*	*Date*	*Age (y)*	*Method*	*Findings*			*Complications*	*Remarks*	*Bone/Air Conduction Hearing Levels (dB HL)*		
						Footplate	*Stapes*	*Mucosa*			*Preop*	*Postop*	*Follow-up*
Immediate hearing loss													
1	F	R	1972	15	Teflon	Very thick	Normal	Bleeding	Floating footplate	Immediate hearing loss	20/53	?/80	57/105
		L	1974	17	Teflon	Solid bony apposition	?	Thick	None	Adhesions; granulations; revision	20/70	?/70	ND/115
2	F	L	1979	25	Teflon	Solid bony; bleeding	Normal	Normal	Perilymph leakage	Immediate hearing loss	27/43	?/88	ND/88
3	F	L	1981	16	Teflon	Enormous, thick apposition	Thin; atrophic	?	Perilymph leakage	Immediate hearing loss	32/53	37/75	67/87
4	M	R	1987	20	Teflon-wire	Very thick	Normal	Normal	None	Immediate hearing loss; revision	10/35	27/38	25/30
5	F	R	1988	27	Teflon-wire	Very thick anterior and posterior walls; soft; bleeding	Normal	Normal	Floating footplate	Immediate hearing loss	17/55	48/65	48/52
Hearing loss at follow-up													
6	F	R	1969	44	Gelfoam-wire	Thick bony anterior and posterior apposition	Thin; atrophic	Thick; bleeding	None	Small oval window niche	52/97	52/57	ND/87
		L	1970	45	Gelfoam-wire	Soft; thick bony anterior and posterior apposition	Thin; atrophic	Thick; bleeding	None	Small oval window niche	53/92	(? Hearing gain)	ND/110
7	M	R	1983	37	Teflon-wire	Normal	Thin; atrophic	Hypertrophic; bleeding	None	Annoying bleeding	30/60	47/47	73/73
8	M	R	1978	22	Teflon	Thick fibrotic layer; bleeding	Thin; atrophic	Thick; bleeding	Posterior part of footplate in vestibulum	Revision after 6 years	18/53	10/15	35/52
9	F	L	1964	36	Teflon	Bony; very thick	?	?	None	Trauma after 8 years; revision	43/80	43/43	ND/90
10	F	L	1963	34	Vein-strut	?	?	?	?	Not successful	?	?	67/77

HL — hearing level, ? — unknown, ND — not detectable.

(Table 7).

The findings and events during operation could be reasons for the ultimately poor result. In the group with an increase in the hearing loss directly after the operation, a solidly thickened footplate, large bony appositions, and an oval window that was difficult to access had a detrimental influence on the operative results in five of six ears. In the group with an increase in the sensorineural compo-

TABLE 10. FINDINGS AT FIVE STAPEDECTOMIES RESULTING IN TOTAL DEAFNESS

Pt	*Sex*	*Study*	*Age (y)*	*Method*	*Findings*			*Complications*	*Remarks*
					Footplate	*Stapes*	*Mucosa*		
11	?	Shea and Postma[39]	?	Piston, ? type	Solid obliteration	?	?	?	Hearing loss within 1 year after revision
12	?	Shea and Postma[39]	?	Piston, ? type	Solid bony apposition	?	?	None	Hearing loss 3 years after revision
13	F	Patterson and Stone[29]	25	Gelfoam-wire	Moderately thickened	Thin; atrophic	?	None	Immediate hearing loss
14	F	Kosoy and Maddox[30]	42	Gelatin-wire	Deep-set; soft mass on anterior edge	?	Normal	Premature stapes mobilization	Immediate hearing loss
15	M	Brosnan et al[32]	47	Piston, ? type	Discrete margin; slight fixation	Normal	Vascular	None	Immediate hearing loss presumably due to surgical trauma

? — unknown.

TABLE 11. MEAN PREOPERATIVE BONE CONDUCTION THRESHOLDS

	Shea and Postma[39]		*Pedersen and Elbrond*[40]		*Others*[5,25,29-35,38]		*This Series*[41,42]		*Presumed Failures*	
Preoperative Bone Conduction	*No. of Ears*	*%*	*No. of Ears*	*%*	*No. of Ears*	*%*	*No. of Ears*	*%*	*No. of Ears*	*%*
0-20 dB	28	45	30	70	15	21	26	45	5	42
20-40 dB	14	23	9	21	3	4	22	38	3	25
40-60 dB	16	26	3	7	0	0	6	10	3	25
60-80 dB	3	5	0	0	0	0	1	2	0	0
80 dB or more	1	2	0	0	0	0	1	2	0	0
Unknown	0	0	1	2	53	75	2	3	1	8
Mean preoperative sensorineural hearing level	—		18.8*		12.2		26.1		29.3	
No. of ears	—		42		18		56		11/56	

Dash — not applicable for lack of data.

*Extrapolation from figures.

nent of the hearing loss 12 months after the operation or later, no causal relationship with the disease or with the middle ear could be established in three of six ears. In the three other ears from this group in which a severe sensorineural hearing loss arose later on, the disease process itself proved to be the cause.

When there is a continuous progression of the sensorineural hearing loss as a result of the bone disease itself, there is a good chance that this will be bilateral. In nearly every nonoperated contralateral ear, an increase in the sensorineural component of the hearing loss could be established if the follow-up period was long enough. In the group of six ears with an increase in hearing loss directly after the operation, a progression of the sensorineural loss still occurred in the follow-up period after the surgical accident.

Considering these data it can be concluded that stapes surgery in osteogenesis imperfecta has more pitfalls than in otosclerosis. The disease process itself leads to changes in the form and structure of the footplate, the stapes superstructure, and the other components of the ossicular chain, so that no two ears show exactly the same picture. That is why more complications are encountered than in the otosclerosis patient. It is remarkable that despite the increased number of complications, there were no deaf ears directly after the operation in this Dutch series of 58 ears, as opposed to other studies.[29,30,32,39] Revision operations proved to be risky, since in only 6 of 19 ears (32%) was a good result achieved.

A notable finding in this study was that a progressive sensorineural hearing loss that is not related to the operation can have an important if not decisive effect on the ultimate result. Not infrequently, an apparently good operative result can be destroyed in the short, but usually longer, term by a severe sensorineural hearing loss. It is unjustified to consider these operations as failures. Frequent postoperative measurement of the bone and air conduction thresholds, even after a good result, is necessary to answer possible questions about hearing loss of later onset. A reliable prediction of the ultimate hearing threshold in the long term is difficult to make because of the progressive inner ear deafness that is associated with the disease process. It is remarkable that the group with disappointing results directly after the operation was relatively young and had a high preoperative bone conduction threshold. All these patients proved to have complication-sensitive changes in the footplate and oval window. It is precisely this risk group that needs the highest care that we can offer, and such patients should only be treated by the most experienced of otologists.

TABLE 12. FINDINGS AT OPERATION IN 5 OF 15 REVISIONS

Pt	*Study*	*Findings at Revision*	*Hearing Result*
16	Opheim[25]	Polyethylene strut too short, replaced by longer one; floating footplate; fat mass under longer strut	Considerable improvement
17	Patterson and Stone[29]	Incus marked with multiple granulomata; granulomatous mass extended from under incus to fill oval window niche	Dead ear
18	Patterson and Stone[29]	Oval window closed with iceberg-type bone	18-dB hearing level
19	Cohen[34]	First revision: Teflon cup piston not found; no fistula; distal part of incus disappeared; TORP between incus and oval window membrane	50-dB air-bone gap
		Second revision: granuloma between shaft of TORP and rim of oval window; TORP trimmed	20-dB air-bone gap

TORP — total ossicular replacement prosthesis.

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SURGICAL COMPLICATIONS WITH THE COCHLEAR MULTIPLE-CHANNEL INTRACOCHLEAR IMPLANT: EXPERIENCE AT HANNOVER AND MELBOURNE

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The surgical complications for the first 153 multiple-channel cochlear implant operations carried out at the Medizinische Hochschule in Hannover and the first 100 operations at the University of Melbourne Clinic, The Royal Victorian Eye and Ear Hospital, are presented. In the Hannover experience the major complications were wound breakdown, wound infection, electrode tie erosion through the external auditory canal, electrode slippage, a persistent increase in tinnitus, and facial nerve stimulation. The incidence of wound breakdown requiring removal of the package was 0.6% in Hannover and 1.0% in Melbourne. The complications for the operation at both clinics were at acceptable levels. It was considered that wound breakdown requiring implant removal could be kept to a minimum by making a generous incision and suturing the flap without tension.

KEY WORDS — cochlear implant, complications, deafness, surgery.

INTRODUCTION

The first University of Melbourne prototype multiple-channel cochlear implant was implanted on Aug 1, 1978. The first Cochlear multiple-channel cochlear implant for clinical trial was implanted on Sept 14, 1982. Since then, 100 implantations using the Cochlear device have been carried out by the Cochlear Implant Clinic at The Royal Victorian Eye and Ear Hospital in conjunction with the Department of Otolaryngology at the University of Melbourne. The results on the first 153 operations at the Medical Academy (Medizinische Hochschule) in Hannover are also included in this paper. Many more Cochlear devices have been implanted by other cochlear implant units. Sufficient experience has now been obtained to assess the results of the operation and analyze the surgical complications.

There are only a few articles in the literature that provide adequate information on the complications of implantation. Thielemeir[1] does, however, report details on the House Ear Institute results. Out of 269 operations there were four cases of wound breakdown. These were attributed to the coil's being too close to the wound edge. Three breakdowns were corrected by a secondary flap and one required explantation. One patient required the removal of the device to correct a cerebrospinal fluid fistula. No other complications, including meningitis or serious infection, occurred. The Institute's significant complication rate was therefore 2%.

Harris and Cueva[2] reported on a case of wound breakdown with exposure of the device (a Cochlear multiple-channel implant). This breakdown occurred with a C incision's being used in a patient with a previous postauricular scar. It was thought that the C incision together with a postauricular scar compromised the blood supply to the flap. The problem was corrected with the rotation of scalp flaps, and the implant was successfully covered.

Cohen et al[3] have conducted an extensive survey of surgeons in the United States implanting the Cochlear multiple-channel device. In the Cohen et al survey 108 of 115 surgeons (94%) responded to a questionnaire. A total of 459 Cochlear devices had been implanted, of which 60% were the standard device and 40% the smaller mini-device that became available in October 1986. There were 55 complications reported, for an overall rate of 12% (Table 1[3]). There were no deaths; there were 23 (5%) major complications and 32 (7%) minor complications. Major complications were those requiring explantation or further operation or causing a significant medical problem. Minor complications either settled spontaneously or with simple measures. On statistical analysis, the complication rate was significantly less for the mini-device, but further analysis suggested that this difference was due to the increased experience of the surgeons, rather than any difference between the devices.

This paper will assess the results of the Cohen et al survey and present the surgical results from the Medizinische Hochschule, Hannover,[4] and the University of Melbourne Cochlear Implant Clinic at The Royal Victorian Eye and Ear Hospital.

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TABLE 1. TOTAL COMPLICATIONS: UNITED STATES EXPERIENCE IN 459 PATIENTS

Complications	*No.*
Flap-related	
Major	
Scalp breakdowns leading to removal of implant	9
Minor	
Local treatment of flap problem	16
Implant-related	
Major	
Meningitis	1
Severe facial nerve stimulation leading to implant removal	1
Compressed electrode	4
Incorrect electrode position	4
Perilymph fistula	3
Exposure of mastoid bowl electrode	1
Minor	
Facial nerve weakness with recovery	8
Minor facial nerve stimulation that was programmed out	3
Minor change of taste	2
Transient dizziness	2
Tympanic membrane perforation that healed	1

Information from Cohen et al.[3]

TABLE 2. TOTAL COMPLICATIONS: HANNOVER EXPERIENCE IN 153 PATIENTS

Complications	*34 Inverted-U Flaps*	*119 Extended Endaural Flaps*
Flap-related		
Major		
Wound breakdown and infection (device removed and reimplanted successfully 3 years later)	1	0
Wound infection, severe but controlled	3	0
Minor		
Infection in wound (uncomplicated)	3	2
Air under flap	0	2
Seroma	1	1
Implant-related		
Major		
Electrode tie erosion of external auditory canal skin	9	
Electrode slippage (radical cavity, device removed)	1	
Increase in tinnitus (persistent)	6	
Facial nerve stimulation	1	
Minor		
Transient facial nerve palsy	3	
Transient taste disturbance	2	
Transient vertigo or imbalance	3	
Preoperative selection		
Failure to implant (ossified scala tympani)	2	

RESULTS

Table 2 shows the complications for the first 153 patients operated on at the Medizinische Hochschule in Hannover. The Table shows that there were wound breakdown problems with the inverted-U flap, which led to the development of an extended endaural flap that was considered to be more satisfactory. Furthermore, the overall complication rate for the first 34 patients was double that of the second 119. This could also indicate not only, as with the American data, that increased surgical experience and expertise is one of the main factors in reducing complications, but also that the extended endaural flap guarantees a more secure healing of the wound. There was one case of flap breakdown, and the device had to be explanted. This patient was reimplanted 3 years later in the same ear. The extended endaural flap was used for the second operation.

There were nine cases in which an electrode tie eroded through the external auditory canal skin. Initially a Dacron tie was placed in the posterior bony external canal wall, a technique originally used by the Melbourne Clinic. In one of the cases of skin and bony necrosis, the exposed electrode lead was pulled out while the patient was cleaning the canal. The same device was successfully reimplanted. The problems with delayed necrosis of the skin of the outer ear canal led to a change in the technique in which the knot was placed on the cortical bone near the mastoid tip, and as a consequence skin breakdown was reduced.

There was one case of electrode slippage at an early stage. This patient had a radical mastoid cavity that had been created for complications from scarlet fever. There was no possibility of fixing the electrode, and because of subsequent infection the device was finally removed. Failure to implant in two patients occurred because of bony tissue in the scala tympani. The opposite cochlea was not implanted because the computed tomographic scan and/or magnetic resonance imaging showed it to be totally ossified as well.

An increase in tinnitus occurred in six patients during electrical stimulation with the prosthesis,[5] but without any influence on performance. In all patients this tinnitus was in the operated ear, but the problem was not so severe that the device had to be removed. In one of the last cases in the Hannover series, facial stimulation occurred at current levels below the comfortable listening level. This was controlled by programming out the electrodes concerned, without any observable effect on speech understanding.

The Melbourne Cochlear Implant Clinic has implanted 97 patients with 100 Cochlear multiple-channel devices. Three patients had two implants. Two had the opposite ear implanted because of poor performance on the first side. The third had the same ear reimplanted because of device failure following the application of a retro-fit magnet overlying a standard device. A total of 100 implan-

TABLE 3. TOTAL COMPLICATIONS: MELBOURNE EXPERIENCE IN 100 PATIENTS

Complications	*No.*
Flap-related	
Major	
Wound breakdown with exposure of package and infection (device removed)	1
Minor	
Infection in wound (uncomplicated)	1
Eyeglass frame pressure	1
Air under flap (transient)	2
Seroma	1
Thick skin flap (persistent 1, transient 7)	8
Keloid scar	1
Implant-related	
Major	
Electrode tie erosion of external auditory canal skin	1
Persistent increase in tinnitus	1
Minor	
Partial electrode slippage	2
Transient facial nerve paralysis	2
Transient taste disturbance	1
Facial or tympanic nerve stimulation	3
Transient vertigo or imbalance	6
Temporary increase in tinnitus	6
Preoperative selection	
Failure to implant (hemorrhage 1, fibrosed scala tympani 1)	2
Anesthetic-related	
Bronchospasm (anesthetic complication)	1

tations have therefore been performed. The surgical complications and adverse effects are shown in Table 3.

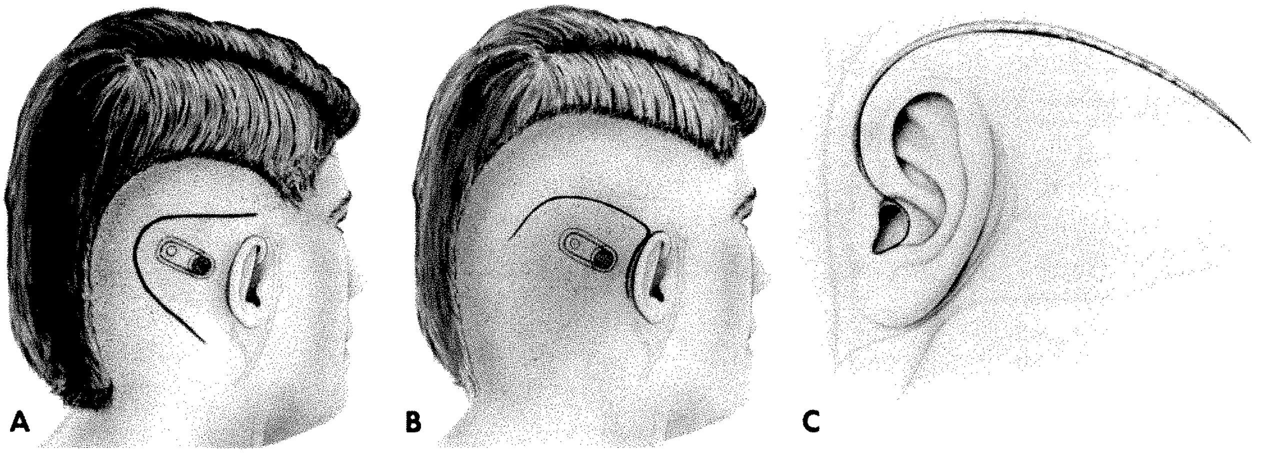
With the University of Melbourne results it is noteworthy that most of the major complications occurred in the early cases. The wound breakdown, however, was later in the series and probably occurred because a small inverted-U flap was used to avoid a ventriculoperitoneal shunt previously inserted for hydrocephalus. During operation a mastoid emissary vein was found that required the package to be implanted higher than expected. In addition, a tie was not placed over the package to immobilize it, and it rotated superiorly. These three factors resulted in the upper edge of the device's pressing on the overlying incision. The wound breakdown was also associated with infection and it is not certain if it was secondary or a causal agent. In addition, it should be noted that the only two cases of infection in the series of 100 operations occurred when the operation was carried out in a day operating room when the main operating room was closed. Although the horizontal laminar flow units providing filtered air were used, the operating room was cramped and crowded and these conditions compromised sterility. The problem of pressure from the side arms of the eyeglass frames on the skin overlying the edge of the package was due to the mini-implant's being placed too far anteriorly. The patient had a serious visual disorder and wore very thick heavy lenses requiring the sides of the eyeglass frames to exert a lot of pressure to hold them in place. In the patient with the excessively thick skin flap, the magnet was unable to hold the external antenna in position. This case was an early mini-implant, and the surgical technique has been revised. Now if the scalp flap is 6 mm thick, the deep fascial flap is not sutured over the antenna section of the implant, or alternatively, it is excised. The patient with the keloid had problems in the siting of the antenna, and the scars required excision.

The fistula in the skin of the external auditory canal was caused by a Dacron tie in the bone of the external canal. A cholesteatoma formed and revision was required. A significant increase in tinnitus occurred after implantation in seven patients. In three this symptom settled in a few days with no treatment other than reassurance. In one patient the tinnitus was associated with an acute anxiety reaction. He had had similar anxiety reactions in the past and this one was rapidly controlled with intravenous diazepam. In three patients the increased tinnitus was more prolonged. All had psychological problems. One had the tinnitus in the operated ear, one had it in the nonoperated ear, and in the third it was widespread. In two of these patients the tinnitus was controlled with psychiatric care and tranquilizers. The other patient, who may have had Munchausen syndrome, attributed several problems such as tinnitus and widespread pain to the presence of the implant, which was otherwise functioning satisfactorily. The implant was eventually removed.

The two cases of partial electrode slippage required a revision operation to push the arrays back to their original position. The slippage occurred because the Dacron ties had not been checked originally. This conclusion was reached when the videotapes of the operations were reviewed.

Three patients had facial and/or tympanic nerve stimulation in some electrodes at a level below the comfortable listening level. This problem was controlled by programming out these electrodes. Other patients had tympanic nerve stimulation from electrodes at or outside the round window. These electrodes had much higher thresholds than the intracochlear ones and were not useful for hearing. Again, they were programmed out and not used in the speech processor.

One failure to implant occurred in a case of severe hemorrhage from a mastoid emissary vein, and the other in a patient who had the scala tympani filled with fibrous tissue. In both cases the opposite side was subsequently implanted successfully. One case of bronchospasm occurred at the induction of anesthesia and was probably due to aspiration of gastric contents.



Incisions. A) C-shaped (Reprinted with permission from Cochlear Corporation Surgical Procedure Manual). B) Inverted-U (Reprinted with permission from Cochlear Corporation Surgical Procedure Manual). C) Extended endaural (Reprinted with permission.[4])

DISCUSSION

Cochlear implantation is a rehabilitative surgical procedure, and ill effects should be minimized. Proper patient selection and care with anesthetic and surgical techniques are both very important. In the three series covered by this paper there have been 712 cochlear implantations performed with the Cochlear multiple-channel prosthesis. There have been no deaths, and the one major medical complication was a case of meningitis that responded well to treatment. There have been a variety of problems occurring at the implant site. Most have been transitory or have responded to local measures. These are temporary inconveniences. Others have required prolonged treatment, revision, or even explantation. These will be considered in detail. In comparing the results obtained in the United States, Hannover, and Melbourne, it should be noted that in Hannover and Melbourne all procedures were performed by a small group of very experienced surgeons, whereas in the United States more than 108 surgeons performed 459 operations.

The most significant complication reported in the three series was wound breakdown. This was a major complication requiring removal of the package in nine cases in the American series (2.0%), in one case in Hannover (0.6%), and in one case in Melbourne (1.0%). In the remaining cases either revision with secondary skin flaps or local measures controlled the problem. In the one Hannover patient with flap necrosis successful reimplantation was carried out 3 years later in the same ear. In the Melbourne case the electrode was left in situ, but the device was removed. This was carried out rather than repairing the defect with a rotation or transposition flap, as a localized pocket of pus was found at revision. The child received a successful reimplantation 6 months later.

In the American series most of the problems were associated with the anteriorly based C-shaped flap (see Figure, A), but as this flap was the one most commonly used it is difficult to determine whether it leads to an increased rate of wound breakdown compared to other designs. Cohen et al[3] emphasize the importance of proper flap design and size, and in particular state that it should be generous, well away from the implant, and sutured without tension. With regard to the C-shaped incision, some surgeons, particularly inexperienced ones, make the flap too small by not placing the incision far enough posteriorly, or by creating an insufficiently broad base. If the inferior limb is taken beyond the inferior margin of the pinna, the blood supply to the flap from the posterior auricular artery may be cut.[2] The combination of a wound sutured under tension over the implant and poor blood supply will lead to flap necrosis. Another pitfall with the C-shaped flap is well described by Harris and Cueva.[2] The C-shaped flap was used in a patient who had had a previous mastoidectomy via a postauricular incision. There was necrosis of the posterior portion of the flap despite hyperbaric oxygen. The necrosed portion sloughed, exposing the device, which was successfully covered with scalp advancement and rotation flaps. They have therefore advocated the use of the inferiorly based inverted-U flap (see Figure, B) in such cases.

The inverted-U flap developed in Melbourne is suitable for the Cochlear multiple-channel implant.[6] This has been satisfactory in the 98 cases in which it was used in Melbourne. In the one patient in whom wound breakdown occurred the incision was compromised because of a verticuloperitoneal shunt. On the other hand, the C-shaped incision was used in two cases in Melbourne. In one the inferior limb cut an unexpectedly large mastoid emissary vein, resulting in a torrential hemorrhage that was extremely difficult to control, and the operation had to be aborted. The inverted-U incision would have allowed better exposure of the emissary vein in order to control the bleeding. In the second case in which the C-shaped incision was used, access to the round window was difficult, and its approach through the posterior tympanotomy was compromised by the C-shaped incision.

The inverted-U incision was used in the first 34 procedures performed in Hannover, but there were four cases of severe wound infection. One of these required revision using a bridge flap, and the other three needed secondary suture after cleaning the wound. The incision was then modified into an extended endaural one (see Figure, C[4]). This incision was used in the next 119 implants, with only two cases of minor wound breakdown, which were controlled with local measures. The reason for the severe infection and flap breakdown with the inverted-U flap in one case in Hannover was the too-early fitting of the device 3 days after operation, when pressure from the original spring headset resulted in necrosis of tissue over the device.

In Hannover and Melbourne we have been meticulous in planning, measuring, and marking the incision in every patient. The care of the flap is also very important. It should not be crushed by instruments and should be kept warm and moist during the procedure. It should be sutured in layers and not under tension. Care must also be taken with any underlying fascial flap.

The problems of erosion of canal skin and fistula formation with Dacron ties placed in the bony ear canal were not related to the flap design. In the early Hannover patients the ties were positioned in the deep part of the outer ear canal, where the skin is very thin and predisposed to breakdown. The technique was subsequently modified so that the tie was placed more externally in the ear canal, where the skin is thicker. Fascia was placed between the skin and the Dacron tie. However, in Hannover, to avoid this problem completely the electrode is now fixed to the back of the bony canal wall with poly maleinate glass ionomer cement (Ketac-cem, ESPE Fabrik Pharmazeutischer Praparate GmbH & Co KG, Seefeld, Germany), used by dentists to fix tooth crowns. This method has been used from patient 145 onward.

In Melbourne, the Dacron tie in the posterior bony canal was abandoned after the first initial series, and for some time reliance was placed on two ties around the thick proximal lead wire. The ties were placed in the mastoid cortex superiorly in the region of the supramastoid crest in the majority, or inferiorly near the mastoid tip. It was also found that if there were only one tie, and this was not made very secure, electrode slippage could occur. To improve the situation and place a tie at a site that would not move in relation to the round window in the growing young child, a technique has been developed in Melbourne by which a platinum multistranded wire is placed around the bridge of bone below the fossa incudis and then crimped around the thin distal section of the lead wire. At the point of fixation the electrode is protected by a Silastic sheath.

In the American series there were cases of electrode compression or misplacement. The misplacement was primarily due to the insertion of the electrode into a hypotympanic cell. These were errors of surgical technique and were a feature of inexperience and insufficient training. Problems with perilymph or cerebrospinal fluid leaks occur typically in cases of congenital abnormalities or skull fractures. In these cases the entry point into the scala tympani should be carefully sealed with fibrous tissue. If necessary the whole middle ear and mastoid must be packed.

Difficulties with eyeglass frames can be avoided if the implant is sited at least 1 cm behind the posterior root of the pinna. Skin flap thickness must also be watched if problems with the magnet are to be avoided. The thickness of the tissue over the antenna should not exceed 6 mm. If this occurs a deep fascial flap should be sutured away from the antenna section or an area of fascia excised. The problem of elevation of the skin flap with nose-blowing can be avoided by packing the aditus as well as the posterior tympanotomy with tissue. It can also be controlled by applying pressure dressings until it has stopped.

No significant injuries to the facial nerve have occurred in any of the cases reported, and this success can be attributed to the overall experience of the otologists performing the operations. However, care must always be taken when carrying out the posterior tympanotomy as well as in avoiding the tympanic membrane and posterior canal skin.

Mastoid emissary veins should be looked for radiographically. If a large one is present the skin flaps and siting of the implant can be adjusted to avoid it. If bleeding occurs it can usually be controlled with pressure, bone wax, or crushed muscle. In one Melbourne case the bleeding was so heavy and persistent that the operation had to be abandoned.

Failure to implant or to stimulate the auditory nerve are largely problems related to the preoperative evaluation, in particular radiography and electrical stimulation of the promontory. Even with abnormal x-ray findings, however, it has been shown that in partially ossified cochleas it is possible to insert electrode arrays for 25 to 26 mm along the scala tympani when the bone, which is situated in the basal turn near the round window, is removed.[7] With more complete fibrosis or ossification of the scala tympani it is possible to enter the scala vestibuli and make the insertion. If both scalae are fibrosed or ossified, a gutter in which the multiple-electrode intracochlear array is placed can be created around the basal turn.[8] Alternatively, extracochlear electrodes could be introduced into separate holes drilled at specific points around the basal turn.[9] Finally, the unpredictable response of tinnitus to treatment applies as much to cochlear implantation as any other treatment modality. It is very important that the patient is made aware of this.

SUMMARY

The complication rates for the 153 implants in Hannover and 100 implants in Melbourne are within acceptable limits. An analysis of the results shows that with attention to detail, complications can be kept to a minimum. Care in the design and management of the flap can also keep wound breakdown to a minimum. The flap must be placed well clear of the margin of the implant, have a good blood supply, be kept moist and warm during operation, and be sutured without tension.

ACKNOWLEDGMENTS — The authors wish to acknowledge support from the State Government of Victoria in establishing the Cochlear Implant Clinic at The Royal Victorian Eye and Ear Hospital. We also thank R. West, President, Cochlear Corporation, for permission to publish the figures of the C-shaped and inverted-U incisions. These were drawn by Ed Zilberts and are from the Cochlear Corporation Surgical Procedure Manual.

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SKULL BASE MALIGNANCY FOLLOWING LONG-TERM SINUS MUCOCELE AND OSTEOMYELITIS

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A case of skull base malignancy following long-term sinus mucocele is presented. While the similarity in clinical signs between sinus mucocele and malignancy has recently been emphasized in the literature, no previous case of skull base malignancy following frontoethmoid mucocele has been reported. The literature is reviewed and the association between inflammatory conditions and sinus malignancy is outlined.

KEY WORDS — frontal sinusitis, mucocele, osteomyelitis, sinus malignancy.

INTRODUCTION

Extensive sinus mucocele represents one of the most challenging conditions treated by otolaryngologists. Several recent reports have discussed the confusion that can arise in differentiating an aggressive mucocele from a sinus malignancy.[1,2] While a sinus malignancy can cause a mucocele by obstructing the sinus ostium, a review of the literature did not identify any cases of skull base malignancy arising at the site of a chronic mucocele.

A case of long-term frontoethmoid sinusitis and mucocele will be presented. The patient required multiple operations and developed extensive osteomyelitis of the frontal, ethmoid, and sphenoid bones. Twelve years after his initial presentation, the patient died of poorly differentiated squamous cell carcinoma of the paranasopharyngeal space and skull base with neck metastasis.

CASE REPORT

The patient was 34 years of age when he first presented to the University of California at Los Angeles Center for the Health Sciences in 1973. He had had a lifelong history of nasal airway obstruction and his condition had been diagnosed as nasal polyposis and chronic sinusitis by a physician 2 years prior to admission. He had undergone bilateral Caldwell-Luc antrostomies in 1972 for the removal of polypoid disease from the maxillary sinuses.

Relevant past history included bronchial asthma that required inhaled bronchodilator therapy. He was allergic to aspirin and penicillin. There was no history of woodworking, smoking, blunt head trauma, or frontal sinus fracture. He worked as a stuntman and was a recreational rodeo rider.

At the time of his first admission, he complained of a 4-week history of increasing right periorbital edema and frontal headaches. Upon evaluation he was found to have pansinusitis with acute frontal sinus disease. Tomograms of the sinuses showed expansion of the frontal sinus margins and an area of posterior table destruction (Fig 1) consistent with mucopyocele. On the third hospital day he underwent right frontal trephination. The patient improved clinically following the operation and a course of intravenous gentamicin sulfate. He was discharged 1 week postoperatively. His physicians planned a course of oral antibiotic therapy followed by a definitive obliterative procedure for the mucocele at a later time.

He did well as an outpatient except for an episode of frontal headaches due to obstruction of the drain. He returned 6 weeks after discharge and underwent a coronal osteoplastic flap operation and obliteration of the frontal sinus with abdominal fat. At the time of the operation he was found to have a large mucopyocele with dehiscence of the orbital roof and the right posterior frontal sinus table.

Despite 4 additional weeks of intravenous antibiotics, the patient continued to have drainage from his trephination site. In October 1973 his frontal sinus was reexplored. A subgaleal abscess and recurrent mucocele were drained and necrotic bone was debrided. He also underwent bilateral Caldwell-Luc antrostomies and a complete ethmoidectomy. Histologic analysis of the surgical specimen demonstrated a mixed inflammatory infiltrate including histiocytes, bone erosion, and necrotic debris consistent with mucopyocele. Acute and chronic osteomyelitis was also present.

The patient was well for 6 months, then developed periorbital cellulitis and multiple sites of purulent drainage from the forehead. He therefore underwent frontal sinus exploration and right transantral ethmoidectomy with drainage of a frontal mu-

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Presented at the meeting of the Paul H. Ward, MD, Society, Palm Springs, California, April 21, 1990.

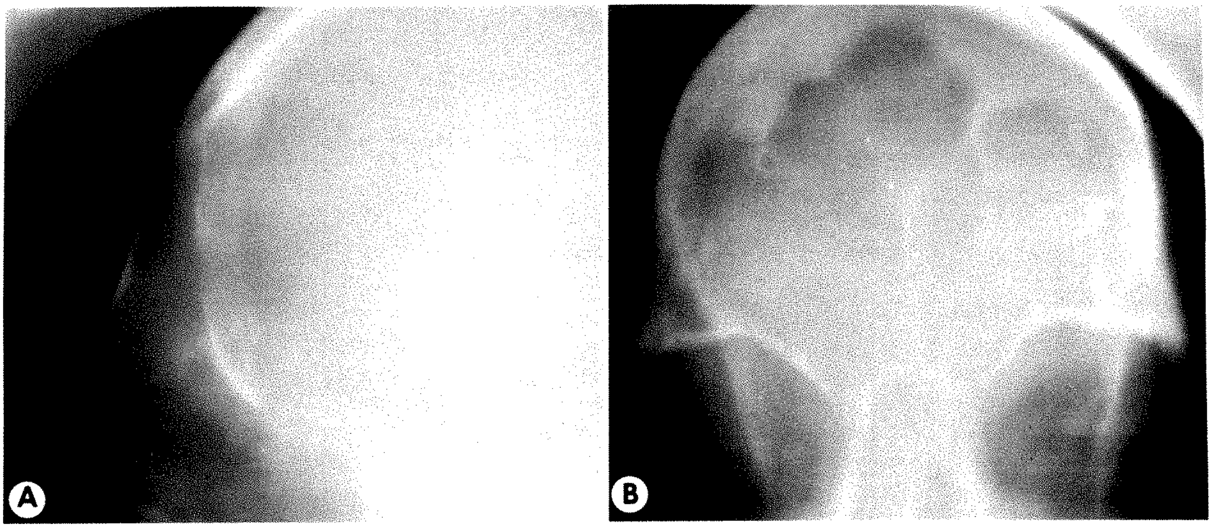

Fig 1. Tomograms taken in May 1973. A) Lateral view shows erosion of posterior table of frontal sinus by mucocele. B) Anteroposterior view shows expansion of frontal sinus with bone erosion.

copyocele in May 1974. The anterior wall and the remainder of the floor of the frontal sinus were collapsed during the procedure.

From 1976 to 1981 he required almost continuous oral antibiotic therapy for chronic sinusitis. He had intermittent drainage from a sinus tract over the right orbit. Polypoid tissue involving the ethmoid and frontal sinus cavities extended into the left orbit, causing chronic proptosis and intermittent periorbital edema.

In June 1981 the patient developed a left orbital abscess, which was drained. One month later a lateral rhinotomy was performed and the remaining bony medial maxilla was resected bilaterally. The patient's course stabilized from 1981 to 1985 and no further sinus surgery was required.

In July 1985 a 3 x 4-cm right neck mass was identified. Fine needle aspiration cytology of the mass suggested lymphoma. Subsequent open biopsy of the neck mass was diagnostic of poorly differentiated squamous cell carcinoma. Multiple biopsies of the upper aerodigestive tract were performed; tissue from the nasopharynx was positive for poorly differentiated carcinoma (Fig 2).

A computed tomography (CT) scan (Fig 3A) showed a soft tissue mass in the right nasopharynx with superior extension to and bony erosion of the skull base. A large additional soft tissue mass without bony erosion (Fig 3B) was identified in the maxillary and ethmoid sinues and nasal cavity, which had been present on several CT examinations over the previous 5 years. Bony dehiscence was present in the posterior frontal sinus, a persistent finding on previous studies (Fig 3C).

The patient was treated with 5,580 cGy to the nasopharynx, skull base, and neck. There was minimal response at both the primary tumor and the neck. The patient died in March 1986 with persistant local and regional disease.

DISCUSSION

This case represents the first report in the literature specifically linking long-term sinus mucocele with the onset of squamous cell cancer of the sinonasal tract and skull base. The literature will be discussed concerning the treatment of mucoceles and the relationship between nasal inflammatory conditions and the development of malignancy.

A mucocele is a chronic expansile condition of the sinus mucosa that contains inspissated mucus. Mucoceles are most often caused by obstruction of the sinus ostia that can occur from inflammatory, iatrogenic, or traumatic causes. Frontoethmoid mucocele presents most commonly with frontal headache (83%) and diplopia (45%).[3] Physical examination frequently reveals frontal tenderness, periorbital swelling, and other ocular findings, as the most common extension of frontoethmoid mucocele is into the orbit. Computed tomography scanning is critical in defining the extent of the disease, including the relationship of the mucocele to the orbital contents and anterior cranial fossa.[3,4]

Treatment of frontoethmoid mucocele involves either resection of the involved tissues with sinus obliteration or marsupialization with adequate drainage to the nasal cavity. Marsupialization is usually preferred, using either the Lynch approach or, more recently, the endoscopic approach reported by Kennedy et al.[4] The preferred treatment for extensive mucoceles with erosion of the posterior frontal sinus table or with anterior cranial fossa extension is a controversial issue.[3,5,6] The patient presented here underwent obliteration of the frontal sinus in the presence of mucopyocele, which is not considered optimal therapy in that setting.[3]

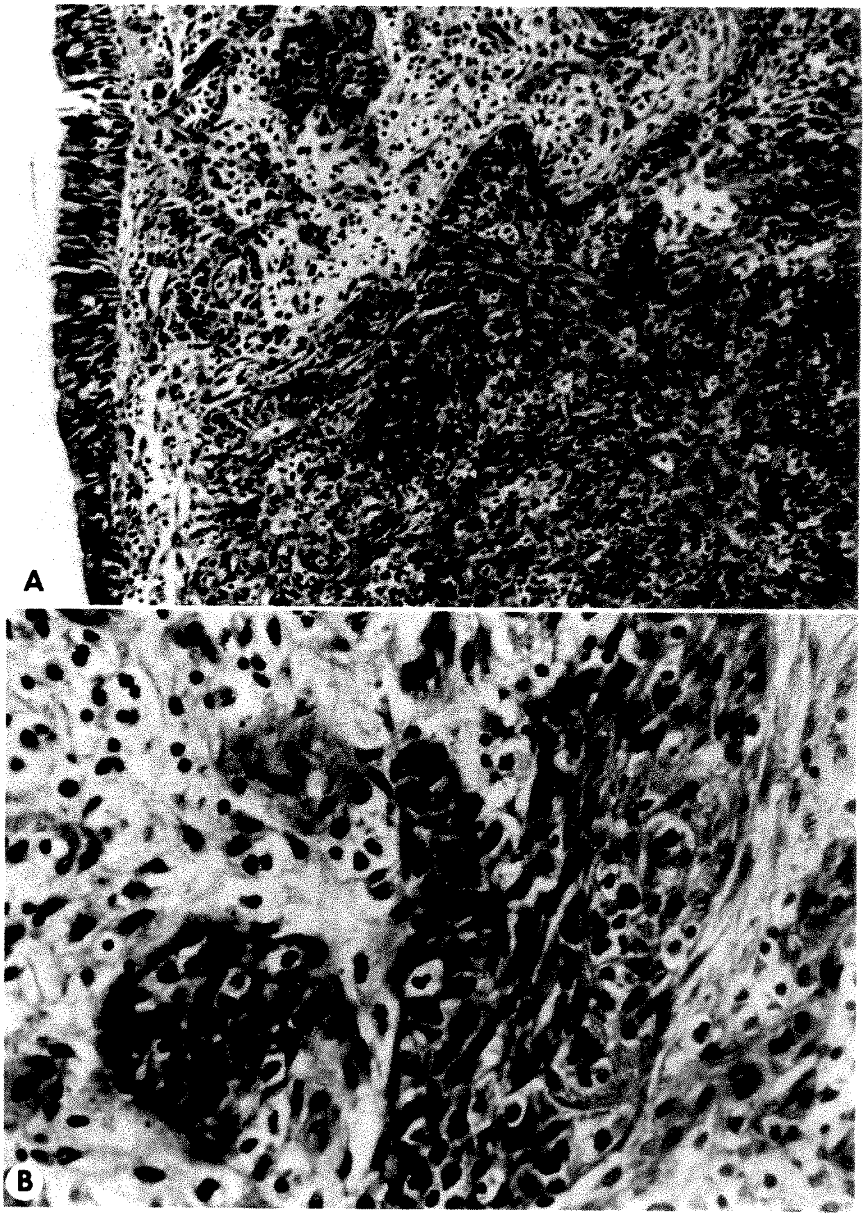

Fig 2. Biopsy of nasopharyngeal tissue. A) Low power shows deeply invasive, poorly differentiated nests of malignant cells. B) High power shows poorly differentiated squamous cell carcinoma.

While the presence of mucocele has not been directly implicated in the causation of sinonasal tract malignancy, an association between malignancy and both chronic sinusitis and osteomyelitis has been documented. The most recent epidemiologic data on sinus malignancy come from Japan, where two separate case-control studies demonstrated an increased risk of developing maxillary sinus cancer in woodworkers and people with a history of chronic sinusitis.[7,8] In one of these two studies, Fukuda et al[7] also found an increased risk of maxillary sinus cancer in patients with a history of nasal polyposis.

The patient presented here had extensive frontal, sphenoid, and ethmoid osteomyelitis. Squamous cell carcinoma occurring in chronic osteomyelitis elsewhere in the body has been frequently documented in the literature. The largest series is from the Mayo Clinic, where 28 cases of malignancy following chronic osteomyelitis were reported, primarily in the extremities. Twenty-five of the cases reported were of squamous cell carcinomas and 3 were of sarcomas. There was usually a long (20- to 30-year) history of intermittent drainage from an epithelial-lined sinus tract with multiple surgical interventions prior to the onset of the malignancy.[9]

Although the malignant transformation of a nasal polyp was the subject of a recent case report,[10] this is considered rare. Inverting papillomas are known to have a higher rate of malignant transformation but are both clinically and pathologically distinct from inflammatory polyposis.[11]

Several authors have emphasized the occasional sinus mucocele that masquerades as a malignancy. Shikowitz et al[1] reported two patients with sphenoid sinus mucocele who presented with multiple

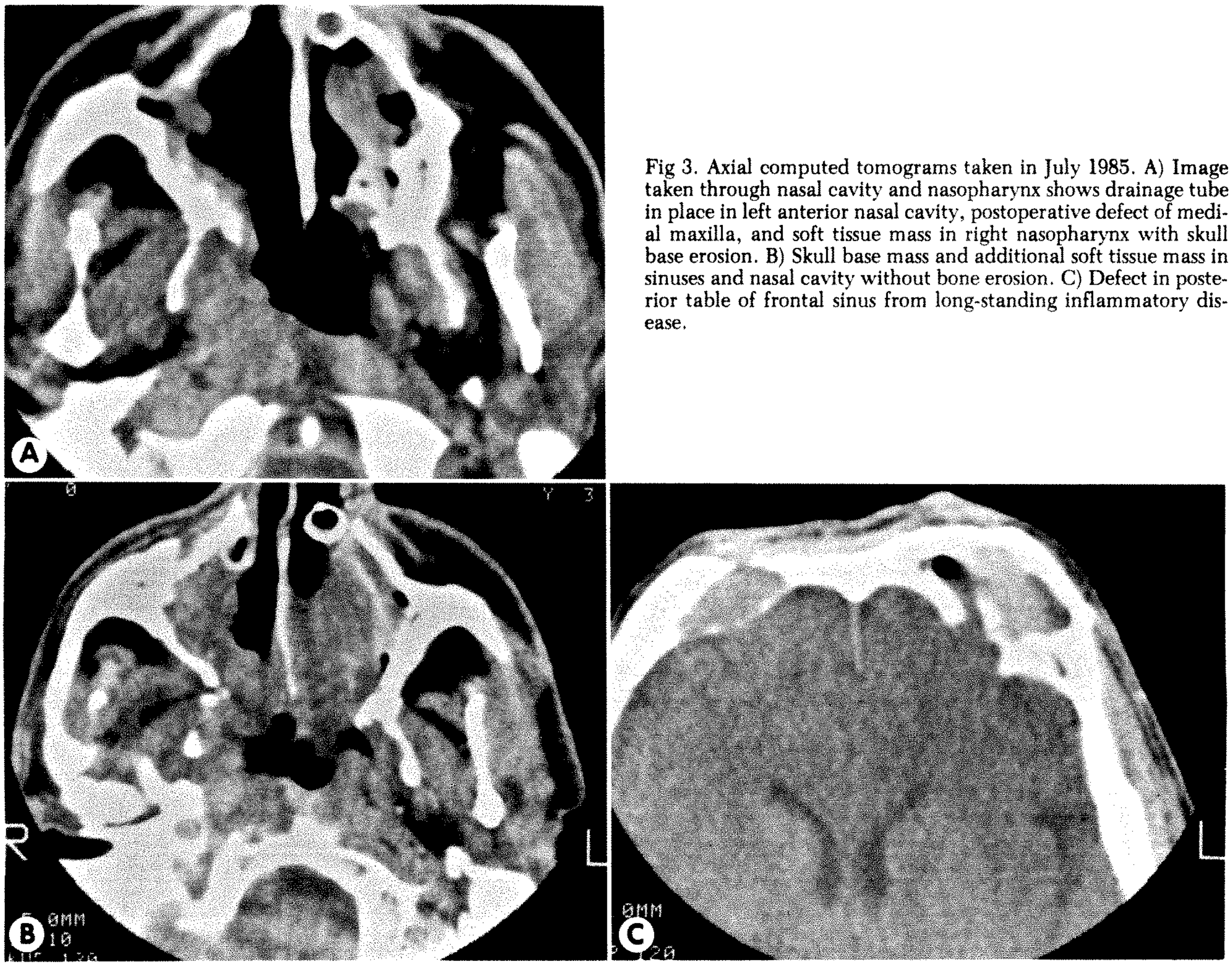

Fig 3. Axial computed tomograms taken in July 1985. A) Image taken through nasal cavity and nasopharynx shows drainage tube in place in left anterior nasal cavity, postoperative defect of medial maxilla, and soft tissue mass in right nasopharynx with skull base erosion. B) Skull base mass and additional soft tissue mass in sinuses and nasal cavity without bone erosion. C) Defect in posterior table of frontal sinus from long-standing inflammatory disease.

cranial nerve palsies and were initially suspected to have malignancies of the skull base.

Other reports have outlined the presence of postobstructive mucocele secondary to cancer. Robinson[2] reported 12 patients with frontal mucocele. With further follow-up, 3 patients were found to have underlying malignancies that caused obstruction of nasofrontal duct drainage. Robinson emphasized that because mucoceles present radiographically as expanding cystic lesions with bony destruction, malignancy should be considered in the differential diagnosis. Brownson and Ogura[12] reported that 48% of patients with epidermoid cancer of the frontal sinus showed bony destruction on sinus radiographs.

This case represents the first report of a chronic frontoethmoid mucocele that preceded the onset of a skull base carcinoma. A causal relationship between the long-term inflammatory disease in this patient and the later malignancy cannot be proven. However, review of the literature supports a relationship between chronic inflammation and later development of cancer.

It is worthwhile noting in this case that the primary neoplasm was recognized only following the development of extensive neck disease. Physicians caring for patients with chronic inflammatory conditions of the sinuses should follow physical findings and CT scans carefully for evidence of malignancy. Although rare, malignant change following long-term sinusitis or mucocele should be kept in mind as a possibility.

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SURGICAL VOICE RESTORATION WITH THE BLOM-SINGER PROSTHESIS FOLLOWING LARYNGOPHARYNGOESOPHAGECTOMY AND PHARYNGOGASTRIC ANASTOMOSIS

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Surgical voice restoration using the Blom-Singer technique is a well-established procedure in patients who have undergone simple laryngectomy. Operations for hypopharyngeal carcinoma are more extensive and require reconstruction using regional skin or myocutaneous flaps, or reanastomosis with colon, jejunum, or stomach. We report the use of the Blom-Singer prosthesis in four patients who had undergone pharyngogastric repair following laryngopharyngoesophagectomy and who had failed to achieve a satisfactory voice. All patients initially developed good speech using the prosthesis. Two patients subsequently had their prostheses removed: one because of recurrent malignant disease and one because the procedure had not significantly altered the quality of the voice. The remaining two patients have continued to use the device at 2 and 5 years after insertion with good voice production.

KEY WORDS — Blom-Singer technique, laryngopharyngoesophagectomy, pharyngogastric anastomosis.

INTRODUCTION

The Blom-Singer voice prosthesis was first described in 1980, with successful voice restoration in 90% of a series of 60 patients treated after laryngectomy.[1] The prosthesis acts as a one-way valve within a surgically created tracheoesophageal fistula, with expired air being shunted into the esophagus while the tracheostoma is occluded. A similar device, described by Panje[2] in 1981, was successful in 20 of 24 patients (83%).

Laryngopharyngoesophagectomy and pharyngogastric anastomosis is an effective and established technique for treating extensive hypopharyngeal carcinoma.[3-5] The procedure was initially described by Ong and Lee,[6] a larger series of 10 patients being reported by Le Quesne and Ranger[7] in 1966. The advantages of using the stomach include its good vascular supply, its ease of suture to the remaining pharynx, and the wide anastomosis that can be made (Fig 1). Rehabilitation of swallowing is rapid and stenosis rare, but speech tends to be reduced in volume and quality. Harrison and Thompson,[3] in a report of a series of 101 cases, state that "the excellent cosmetic result of pharyngogastric anastomosis coupled with relatively trouble free eating is however associated with a poor 'gastric voice.' A small number of patients acquired an adequate voice, but these either had a small pharyngogastric opening or manually compressed the cervical stomach while speaking."

The additional use of a Blom-Singer prosthesis in those patients who fail to develop an effective voice after pharyngogastric anastomosis should act to improve the power, quality, and duration of the voice. The case reports that follow describe the assessment and results in four such patients.

MATERIALS AND METHODS

The ear, nose, and throat unit at Charing Cross Hospital has run a surgical voice restoration program for nearly 8 years. During that time approximately 300 patients have been assessed for voice restoration using the Blom-Singer prosthesis if they have failed to develop satisfactory speech (either esophageal or "gastric" voice) following laryngectomy or pharyngolaryngectomy.

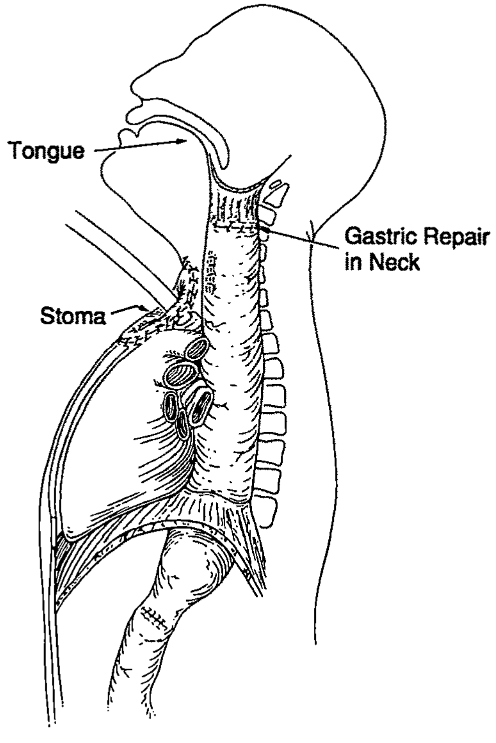

Fig 1. Anatomic diagram illustrating wide pharyngogastric anastomosis in neck.

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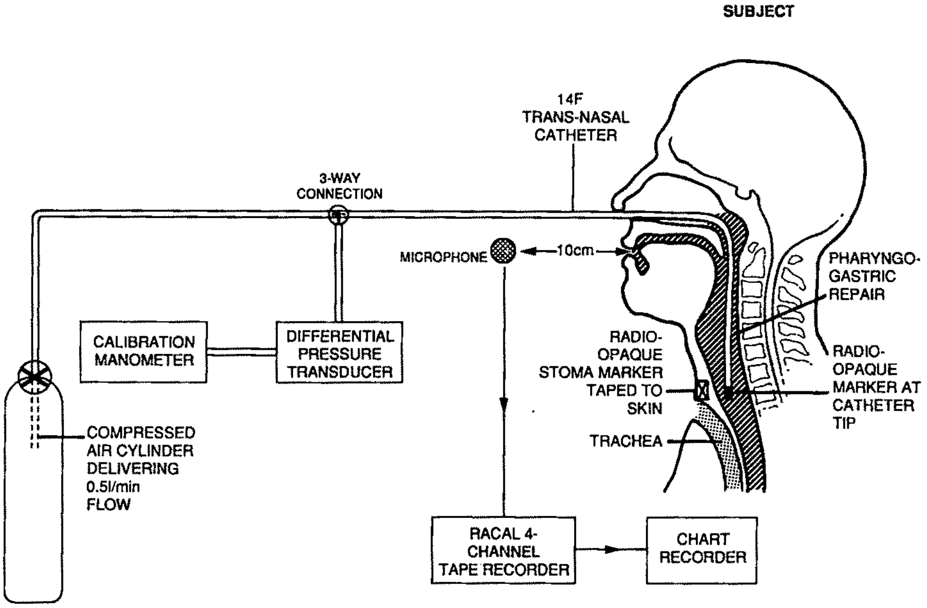

Fig 2. Equipment for measuring pressure and speech acoustics during videofluoroscopic assessment, illustrating placement of nasal catheter.

The standard assessment of these patients has comprised full speech therapy assessment followed by videofluoroscopic assessment of swallowing, voluntary phonation using esophageal or gastric speech, and attempted phonation during an insufflation test. During videofluoroscopy there is joint assessment of the patient by a consultant radiologist, a senior speech therapist, and a head and neck surgeon. Following this assessment, treatment options are discussed with the patient.

Videofluoroscopy is performed as described by Blom[8] and initially involves a contrast swallow study using a low-viscosity medium (Baritop 100: 100% wt/vol barium sulfate). This medium coats the pharynx and pharyngogastric anastomosis, defining the anatomy and any area of obvious spasm or stricture. Voluntary phonation is then attempted, and the vibrating segment (pharyngoesophageal or pharyngogastric segment) is assessed for its presence or absence, its site, and its effectiveness in speech production. Voice is further assessed by the insufflation test.[1,9-11] Air from a compressed air cylinder is passed into the transposed stomach (in cases with pharyngogastric repair) at a rate of 0.5 L/min via a 14F transnasal catheter. The patient then attempts to speak using the air introduced via the catheter (rather than swallowed and regurgitated air) in order to simulate the presence of a Blom-Singer prosthesis diverting expired air into the stomach from the trachea.

Blom et al[10] recommend placing the catheter tip at 25 cm from the nares. Baugh et al[11] found catheter length to matter little, provided the catheter extended into the upper esophagus but not into the stomach (in standard laryngectomy patients). They undertook insufflation at 23- and 25-cm catheter lengths as measured from the nares. We feel that catheter placement should be precise and hence the catheter is passed transnasally under radiographic control until it is positioned opposite the tracheostoma, with use of the radiopaque catheter tip and external stoma site marker to ensure accuracy (Fig 2). This practice enables air to be introduced at the level of the stoma, which corresponds to the site of the proposed Blom-Singer prosthesis. If a vibrating segment is visible radiographically, it is also important to ensure that the catheter tip lies inferior to it so that a voice can be produced.

Both videofluoroscopy recordings and representative single radiographs are retained to provide a permanent record. Since this study, we have been measuring neoglottic opening pressures on phonation during the insufflation test as shown in Fig 2, but these data are unavailable for the patients presented. Although 300 patients have been assessed to date, only 5 patients with laryngopharyngoesophagectomy and pharyngogastric anastomosis have been referred for voice restoration. One patient died before insertion of a prosthesis was possible, leaving 4 patients; it is this small subgroup that we discuss in this paper.

CASE REPORTS

Case 1. In 1980, a 55-year-old man presented with progressive dysphagia and right-sided otalgia, and indirect laryngoscopy demonstrated edema and ulceration of the right hypopharynx. Subsequent direct laryngoscopy confirmed the presence of a large tumor involving the right vallecula, posterior pharyngeal wall, postcricoid region, and upper esophagus. Biopsies gave a histologic diagnosis of squamous cell carcinoma. A laryngopharyngoesophagectomy and pharyngogastric anastomosis was performed, with a feeding jejunostomy to protect the suture line. The postoperative course was uncomplicated and the patient underwent regular outpatient review.

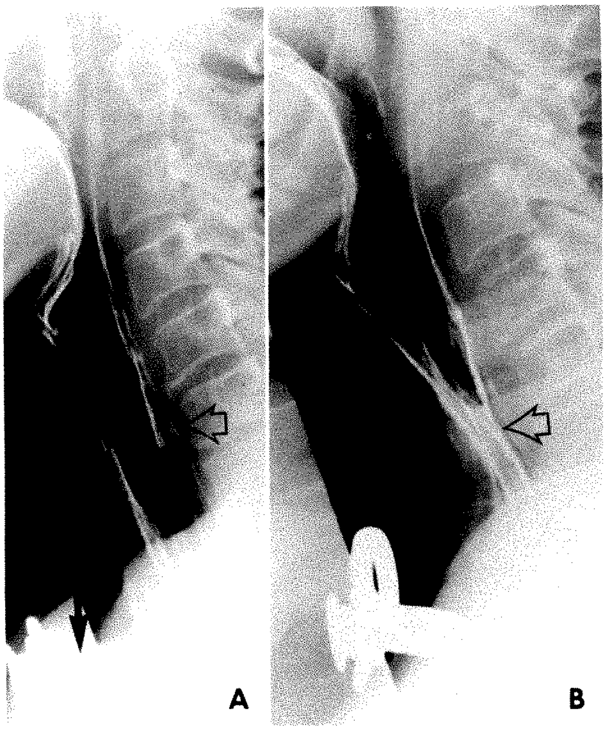

Fig 3. (Case 2) Radiographs of patient. A) Attempting phonation, illustrating absence of effective vibrating segment (open arrow), and position of tracheostomy tube (solid arrow). B) Applying external digital pressure on phonation to create vibrating segment (arrow).

In 1982 the patient was referred to Charing Cross Hospital for speech therapy assessment. The main complaint was that the voice was both too quiet and of poor quality, particularly immediately after eating. Videofluoroscopy showed a poorly defined pharyngogastric vibrating segment, and an insufflation test gave equivocal results in terms of passive speech production because of difficulty in inflating the large distensible reservoir formed by the stomach; this difficulty resulted in problems in maintaining a good vocal tone. It was also noted that the patient had a small tracheostoma and that he was worried by the necessity to repeatedly occlude the stoma with a finger to achieve voice.

Early in 1983 a tracheogastric puncture was performed under general anesthesia and a 14F nasogastric tube was inserted to maintain the fistula. Four days later, good "open tract" voicing was obtained (with use of exhaled air diverted through the open fistula without the prosthesis in situ), but subsequent fitting of the Blom-Singer prosthesis proved difficult because of the small tracheostoma.

A stoma reconstruction was therefore required, following which a second tracheogastric puncture and Blom-Singer prosthesis fitting was undertaken. A good voice was obtained with additional external digital pressure to create an effective vibrating segment, and the patient was pleased with the result.

Unfortunately, the patient was involved in a traffic accident approximately 1 year later and the prosthesis was inadvertently removed at an emergency room elsewhere. A further tracheogastric puncture and fitting of a prosthesis was therefore necessary. The initial 2.6-cm valve was downsized to 2.2 cm after postoperative edema had settled and a good voice was obtained. The patient was satisfied with both the prosthesis and voice, and was discharged.

One further tracheogastric puncture and fitting was required after the prosthesis "fell out," but since that time there have been no problems. At his last review, 5 years from diagnosis, the patient was well with no sign of recurrence and was using the Blom-Singer valve to communicate intelligibly.

Case 2. A 53-year-old man underwent laryngopharyngoesophagectomy in 1981 for a large, ulcerating tumor of the right pyriform fossa that extended inferiorly into the cervical esophagus. Histologic examination of the specimen confirmed poorly differentiated squamous cell carcinoma.

He was referred for possible Blom-Singer prosthesis insertion in 1985, but was found to have a right middle lobe pneumonia on admission. This disease required treatment with antibiotics and physiotherapy, and resolved without any evidence of an underlying second primary lung tumor.

Videofluoroscopy and insufflation assessments confirmed the hypotonic picture typical of gastric repair (Fig 3A), with no significant vibrating segment unless external pressure was applied. A tracheogastric puncture and subsequent fitting of a 2.2-cm Blom-Singer prosthesis was successfully performed in December 1985. A good voice was obtained although a somewhat gurgling quality persisted. Six months later the patient was well, with no sign of recurrence and with a good voice.

Within 3 months, problems in using the prosthesis developed. The patient was tending to use short bursts of injected air, then intermittent external digital pressure on the neck to produce short phrases. There was also air leakage from around the stoma while he was using the valve, and excessive mucus production that both blocked the prosthesis and crusted around the outer housing.

Speech was improved by training the patient to occlude the stoma effectively with the thumb of the right hand to prevent air escape. In addition, the right index finger was used to press against the left side of the neck to provide external resistance and hence to define a vibrating segment and increase the loudness of the voice (Fig 3B). On review in 1987 the patient had remained well and was using the prosthesis to communicate effectively.

Case 3. A 61-year-old woman was referred for assessment in 1986, having undergone radiotherapy followed by laryngopharyngoesophagectomy 4 months previously for postcricoid carcinoma. There was a preceding history of carcinoma of the bronchus, treated by lobectomy and postoperative chemotherapy. The long-term prognosis was therefore extremely poor.

The videofluoroscopic assessment showed a markedly hypotonic appearance typical of gastric pull-up repair, but a good voice was obtained on the insufflation test when external digital pressure was applied to the side of the neck. The tracheostoma was also noted to be very small, probably requiring revision for effective use of the Blom-Singer prosthesis.

Accordingly, in January 1987, the patient underwent stoma reconstruction to increase tracheostomal size, together with a bilateral sternomastoid tenotomy to correct the deep recession of the stoma. A tracheogastric puncture was also performed and the fistula maintained with a 14F nasogastric tube. Two days later a 1.8-cm low-pressure prosthesis was fitted, with a modified size 8 Bivona stoma vent in situ to prevent stoma contraction.

There were initial minor problems with local infection around the tracheostoma with edema, redness, and discomfort, but these subsided rapidly with wound care, suction, and antibiotics. The patient required repeated tuition and reassurance in the use of her Blom-Singer prosthesis, but within a week was producing a good clear voice and was coping well.

On review at 3 months the prosthesis was changed. The patient was managing well, but complained of feeling constantly tired and lethargic, with the valve being an effort to use. Two weeks later the patient developed increasing malaise with a chronic cough, vomiting, and weight loss. She requested removal of the prosthesis at her local otolaryngology department in an attempt to reduce the cough, and subsequently her condition temporarily improved. However, within 6 weeks there was further relapse and the patient became largely confined to bed. Recovery never reached a stage at which repeat puncture and reinsertion of a prosthesis seemed reasonable, and the patient died of disseminated carcinoma with multiple lung secondaries and tracheal recurrence at the end of 1987.

Case 4. A 56-year-old man was referred for possible insertion of a Blom-Singer prosthesis in 1983. He had undergone laryngopharyngoesophagectomy and pharyngogastric anastomosis for postcricoid squamous cell carcinoma in 1979, at the age of 52. However, he had never developed reasonable speech and had, as a consequence, suffered marital problems and become unemployed.

The main complaint was of regurgitation of stomach contents on attempting loud speech. The videofluoroscopy assessment confirmed hypotonicity, but the gastric voice was good and improved further with digital pressure over the neck. The air insufflation test, however, produced no voice at all, and digital pressure made no improvement. This problem was thought to be due to inability to inflate the stomach with sufficient air.

Because of the above findings the patient was first advised to try an external pressure band in an attempt to improve the tonicity of the vibrating segment by providing anterior resistance to the hypotonic and distensible stomach. Two weeks later the patient was reassessed and the voice had improved significantly in quality.

Despite the obvious improvement with the pressure band, the patient was eager to try the Blom-Singer prosthesis. In May 1984 a tracheogastric puncture was performed and the fistula maintained with a 14F nasogastric tube. Five days later, a 3.0-cm prosthesis was fitted and a good voice was obtained. Within 2 weeks the patient was using the prosthesis well, but at 2 months there were problems in using the outer tracheostoma valve (a self-adhesive plastic ring and push-fit "flutter-valve" unit that obviates the need for finger occlusion of the stoma to produce speech). Use of the outer valve was therefore discontinued.

Four months after fitting of the prosthesis the patient was using the index finger to occlude the stoma and produce speech, and he was progressing reasonably. He was, however, unimpressed with his voice, which remained gastric in quality. Two months later he underwent speech therapy and had hardly been using the prosthesis. At his request it was removed, and the fistula closed rapidly and spontaneously without leakage of gastric contents into the tracheostoma. No further follow-up was arranged.

RESULTS

All four patients in this series developed good voice with the Blom-Singer procedure. The characteristics of speech before and after the fitting of a Blom-Singer prosthesis are summarized in Table 1. The increased airflow through the prosthesis improved both the loudness and duration of speech, although in one patient the subjective quality of the voice did not improve significantly. The persistent gastric quality caused that patient to discontinue the use of the prosthesis. The other patient failure was due to general debility with chronic cough (a category of patient noted by McConnel and Duck[12] to be poor candidates for tracheoesophageal speech rehabilitation), and this failure was followed by rapid recurrence of malignant disease that precluded further attempts at surgical speech rehabilitation. It must be emphasized, however, that all four patients had failed to develop effective communication with standard speech therapy following their operations, and that each patient quickly developed clear speech after insertion of the prosthesis.

TABLE 1. SPEECH CHARACTERISTICS BEFORE AND AFTER BLOM-SINGER PROCEDURE IN PATIENTS WITH PHARYNGOGASTRIC REPAIR FOLLOWING LARYNGOPHARYNGOESOPHAGECTOMY

	Pre–Tracheogastric Puncture				*Post–Tracheogastric Puncture*			
	Pt 1	*Pt 2*	*Pt 3*	*Pt 4*	*Pt 1*	*Pt 2*	*Pt 3*	*Pt 4*
Mean duration of vowel sound /a/ (seconds)	0.5	0.5	<0.25	<0.25	5	8	6	9
Syllables per breath (expired) in connected speech	2	1	1	2	15	12	9	10
Voice quality	All subjects poorly intelligible with breathy, "gurgly" voice quality				All subjects improved in intelligibility and loudness (subjective reports)			

DISCUSSION

Patients who have undergone laryngopharyngoesophagectomy have had extensive surgical resection. Pharyngogastric anastomosis, although providing a reliable repair with rapid rehabilitation of swallowing, does tend to produce a voice of little power and of "gurgling" quality. Speech production after gastric repair is difficult because the large, flaccid stomach fails to develop a true pharyngogastric vibrating segment. The voice therefore tends to be weak and whispery, and has an additional gurgling quality due to the liquid gastric content that is particularly noticeable after meals.

This weak, gurgling voice may be improved by external digital pressure over the neck, which creates an effective pharyngogastric vibrating segment or pseudoglottis.[13] Similarly, by using an applied device such as the Dan Kelly pressure band, a simple Velcro elastic strap, or even a tight shirt collar or stoma bib tape, anterior resistance over the vibrating segment is improved.[14] All these methods are useful in preventing ballooning of the flaccid gastric segment, hence improving the apposition of the walls of the stomach and defining a pharyngogastric vibrating segment. A comparison of different vocal mechanisms following laryngeal operations is illustrated in Table 2.

These four patients, who failed to develop adequate speech following laryngopharyngoesophagectomy and pharyngogastric anastomosis, are analogous to the hypotonic group of failed esophageal speakers described by Cheesman et al.[15] All showed a typically hypotonic appearance on videofluoroscopy, with little or no effective vibrating segment. On insufflation testing, three patients had a weak voice and one patient failed to produce any voice at all. (This failure was thought to be due to progressive dilatation of the stomach.) Despite these findings, all four patients produced effective speech following insertion of a Blom-Singer prosthesis, but all required additional external compression to approximate the walls of the stomach and create an effective vibrating segment. Three patients used digital pressure, and one an external pressure band.

The routine use of the insufflation test as part of a standard investigation protocol would therefore seem to be of limited value in the small subgroup of patients with pharyngogastric repair. The stomach forms a flaccid, distensible reservoir that expands progressively on insufflation (unlike the esophagus), and there is often no well-defined neoglottis unless external digital pressure is employed (Fig 3). The main value of the insufflation test is in assessing degrees of hypertonicity in the reconstructed pharynx after standard laryngectomy (hypertonic, stricture, and spasm groups[15]).

A similar situation to that seen after gastric repair was noted by Wolfe et al,[16] who found evidence of poor lower esophageal sphincter function (hiatus hernia or gastroesophageal reflux) in seven patients with poor esophageal speech. They postulated that the esophagus depended on a competent distal sphincter in order to act as an effective air reservoir for speech production. Similarly, Baugh et al[11] found the insufflation test ineffective if the nasal

TABLE 2. COMPARISON OF VOCAL MECHANISMS FOLLOWING LARYNGECTOMY

		Surgical Procedure Performed			
Vocal Mechanism	*Normal*	*Laryngectomy*	*Laryngectomy With Blom-Singer Prosthesis*	*Laryngopharyngoesophagectomy With Pharyngogastric Anastomosis*	*Laryngopharyngoesophagectomy and Pharyngogastric Anastomosis With Blom-Singer Prosthesis*
Initiator	Air from lungs	Regurgitated air from esophagus	Air from lungs via prosthesis	Regurgitated air from stomach (gastric reservoir)	Air from lungs via prosthesis
Vibrator	Vocal cords	Pharyngoesophageal segment	Pharyngoesophageal segment	Pharyngogastric vibrating segment	Pharyngogastric vibrating segment
Resonators	Oropharynx, nose, mouth	Oropharynx, nose, mouth	Oropharynx, nose, mouth	Oropharynx, nose, mouth	Oropharynx, nose, mouth
Articulators	Tongue, teeth, lips, palate	Tongue, teeth, lips, palate	Tongue, teeth, lips, palate	Tongue, teeth, lips, palate	Tongue, teeth, lips, palate

catheter extended more than 27 cm from the nares, because gastric insufflation resulted. Gastric pull-up patients have no lower esophageal sphincter — only a large, flaccid stomach that tends to distend progressively. It is this factor, together with the lack of an effective vibrating segment, that causes such difficulty in speech production.

The Blom-Singer prosthesis is of proven benefit in the rehabilitation of voice after laryngectomy. It is a relatively simple technique and has been used both as a primary procedure at the time of laryngectomy[17,18] and as a secondary procedure in patients who have failed to develop esophageal speech. The use of the Blom-Singer voice prosthesis in patients who have required gastric pull-up repair appears to be similarly effective, and to our knowledge this application has not been previously described. We conclude that use of the Blom-Singer voice prosthesis is an effective method of surgical rehabilitation of speech following laryngopharyngoesophagectomy and pharyngogastric anastomosis.

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ULTRASTRUCTURAL EVIDENCE OF A MEROCRINE SECRETION IN THE HUMAN ENDOLYMPHATIC SAC

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The results of a light and transmission electron microscopic analysis of an endolymphatic sac (ES) from a patient suffering from episodic vertigo, tinnitus, and hearing loss are presented. A biopsy of the intraosseous portion of the ES was obtained during a translabyrinthine approach to section the vestibular nerve in the internal acoustic meatus. The material consisted mainly of tubular epithelial structures filled with heavily stained material. Pathologically dilated and degranulated rough endoplasmic reticuli and disaggregation of polyribosomes with accumulation of solitary ribosomes in the cytosol and endoplasmic reticulum suggested a disturbed epithelial cell protein synthesis. Ultrastructural evidence of an increased merocrine secretion of glycoprotein conjugates into the ES was noted. This made it possible to analyze the presumed intracellular secretory pathways. An increased number of intraepithelial lymphocytes and monocytes was observed. Since the inner ear had been subjected to surgical intervention before the vestibular nerve section, no conclusions can be drawn as to whether the patient's symptoms were related to the disturbed protein metabolism and hypersecretion of glycoprotein conjugates into the ES. The findings support earlier experimental results that indicate that the ES has not only a resorptive function but also a secretory one.

KEY WORDS — endolymphatic sac, merocrine secretion, ultrastructure, vertigo.

INTRODUCTION

The exact function of the human endolymphatic sac (ES), as well as its role in the pathogenesis of Meniere's disease, is still unclear.[1,2] The ES is believed to resorb endolymph, and it may also be involved in phagocytosis,[3,4] immunodefense,[5,6] and pressure regulation[7,8] of the inner ear fluids. This paper presents the results of a light and electron microscopic analysis of an ES from a patient with episodic vertigo, tinnitus, and hearing loss. Meniere's disease was suspected. Because the ultrastructural patterns of the ES are unusual and may provide additional information on the biologic function of the ES, they are presented in detail.

MATERIALS AND METHODS

A 44-year-old woman had an onset of right-sided hearing loss, tinnitus, and ear pressure in 1983. She also experienced intermittent dizziness, but whether it was related to these symptoms in the right ear could not be established. Meniere's disease was suspected. She suffered frequent migraine and tension headaches, sometimes associated with dizziness and often with emotional upsets. She took estrogen since having a hysterectomy and oophorectomy in 1962. The patient underwent a right-sided stapedectomy elsewhere because of suspected otosclerosis. After this procedure the patient was deaf in that ear; vertigo subsided, but dysequilibrium was chronic. One year after the stapedectomy, the patient was referred to the Otologic Medical Group in Los Angeles, Calif, where she underwent a translabyrinthine vestibular nerve section.

During this procedure the vestibular aqueduct (VA) was identified near its external aperture in the posterior cranial fossa. With a small diamond bur, the VA was skeletonized, with a thin rim of bone left around its circumference. The VA was followed toward its interior opening in the vestibule. With small scissors the dura was cut near the external orifice of the VA. The dura was cut at the petrous surface, close to the external aperture of the VA.

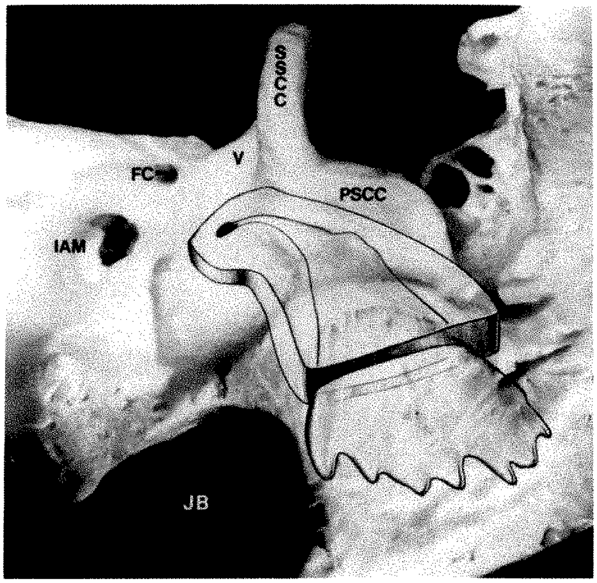

Fig 1. Microdissection of right human temporal bone (posteromedial view). Outline shows area removed for histopathologic studies of endolymphatic duct and sac. IAM — internal acoustic meatus, FC — facial canal, V — vestibule, SSCC — superior semicircular canal, PSCC — posterior semicircular canal, JB — jugular bulb.

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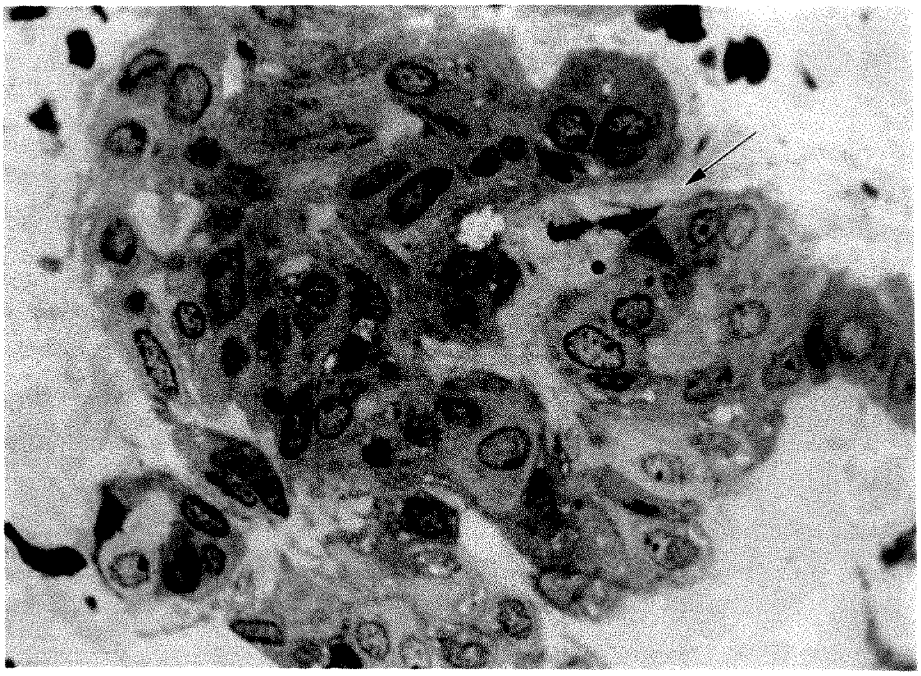

Fig 2. Light micrograph of human endolymphatic sac (original x600). Many epithelial cell nuclei display prominent nucleoli. One cell (arrow) is in mitosis.

The tissue block (Fig 1) was removed and immediately immersed in cold 3% buffered glutaraldehyde. The tissue was decalcified and processed for light microscopy and transmission electron microscopy (TEM) according to a procedure previously described.[9] The vestibular nerve and the sensory regions of the vestibular organ were saved and processed for light microscopy and TEM. The ultrastructural findings of the ES were compared to previous results from cadaver material[10] and four biopsy specimens of the entire intraosseous ES from patients undergoing acoustic tumor removal (H. Rask-Andersen, F. H. Linthicum, Jr, and W. F. House; unpublished data, 1988).

RESULTS

Light Microscopy. The ES consisted mainly of tubular structures that were filled with a heavily stained precipitate. The epithelial cells varied greatly in shape, size, and stainability. In most cells some parts of the cytoplasm were metachromatically stained, especially in the supranuclear region. Cell nuclei frequently contained prominent nucleoli, and a few cell mitoses were observed (Fig 2). The ES was surrounded by both loose and dense connective tissue with a normal appearance and a normal pattern of vascularization.

Electron Microscopy. The present ultrastructural study showed no clear signs of perisaccular ischemic fibrosis. The vascularization appeared normal, with normal blood vessels and without unusual deposition of collagen. Similarly, the lumen of the sac was without deposition of collagen, and there was no evidence of epithelial denudation or atrophy, as has also been demonstrated earlier.[11]

Transmission electron microscopy showed that the general cytoarchitecture of the epithelium as

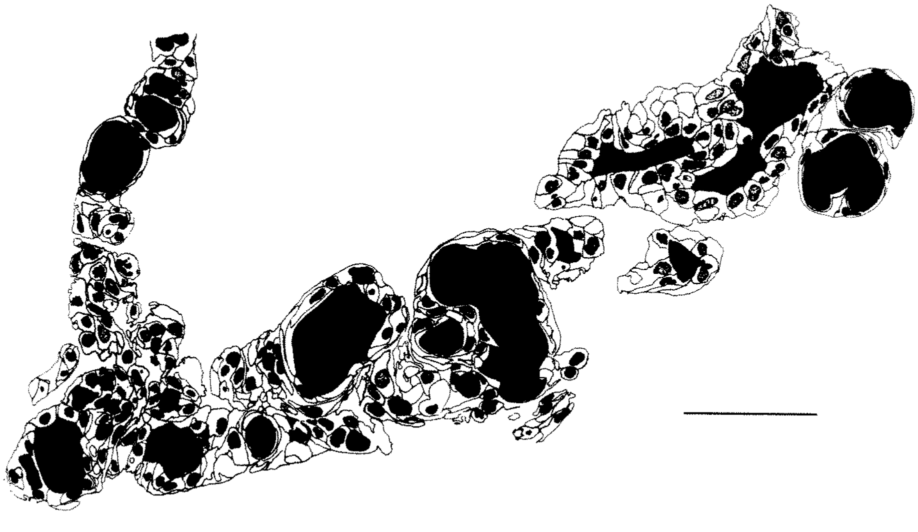

Fig 3. Graphic reconstruction of low-power transmission electron micrograph demonstrating epithelial cytoarchitecture. Sac consists mainly of epithelial tubules that contain homogeneous substance (colored black). Bar — 50 μm.

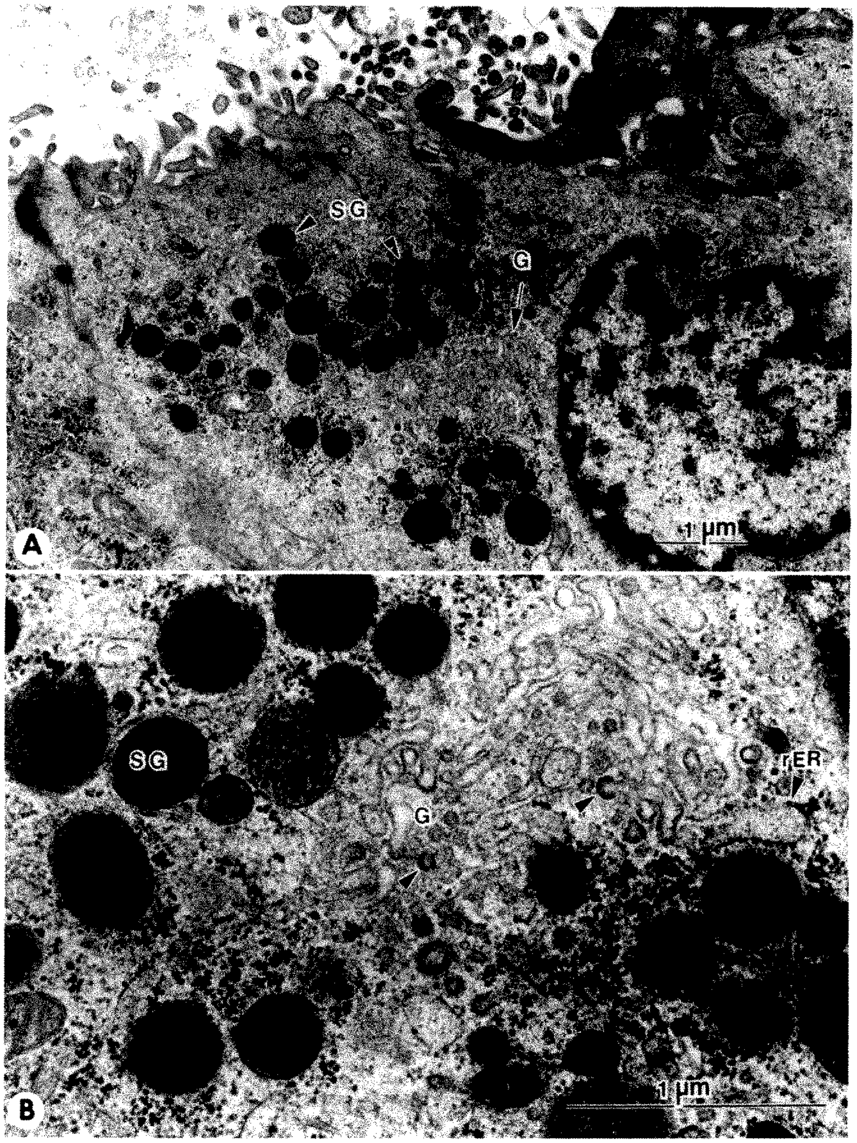

Fig 4. Transmission electron micrographs. SG — secretory-like granules, G — Golgi complex. A) Endolymphatic sac epithelium showing juxtanuclear G associated with membrane-bound SGs (original x17,000). B) Higher magnification of G showing numerous coated vesicles close to Golgi sacs (arrowheads) (original x47,000). rER — rough endoplasmic reticulum.

well as the fine structure of the cell interior, such as the organellar organization, were conspicuously changed (Fig 3) compared to the reference material. Epithelial tubules were filled with an organic material of high electron density. This filling had resulted in a dilatation of the tubules that apparently flattened the epithelial cells.

Irregular cell masses containing numerous tubules or "mini-tubules" of various small sizes were filled with a homogeneous substance. They apparently represented new tubules continuously being formed through active secretion and deposition of organic material among individual cells in areas of epithelial cell proliferation. During secretion, these tubules seemed to enlarge and to be in a state of continuous, prolific change. The apical portion of many of these cells contained membrane-bound, densely stained, secretory-like granules that were closely associated with a well-developed Golgi complex, polyribosomes, and moderately developed rough endoplasmic reticulum (rER) (Fig 4). More material inside the granules was homogeneously stained and of high electron density. A few granules showed a texture of concentric, unit membrane–like layers formed around a central structure of less electron density (Fig 5).

Unlike in the reference material, several membrane-bound granules could be seen to be opening up and discharging their contents into the interior of the tubules (Figs 6 and 7B). The unit membrane surrounding the granules was frequently seen to be close to merging with the apical plasmalemma before membrane separation ultimately led to exocytosis (Fig 7A).

In comparison to the cadaver material, the cell nuclei showed a different chromatin pattern with an increased proportion of euchromatin. Prominent nucleoli were often observed, sometimes associated with a granular nuclear body (Fig 8).

Many cells were undergoing degeneration. Cell membranes had ruptured and cell contents floated

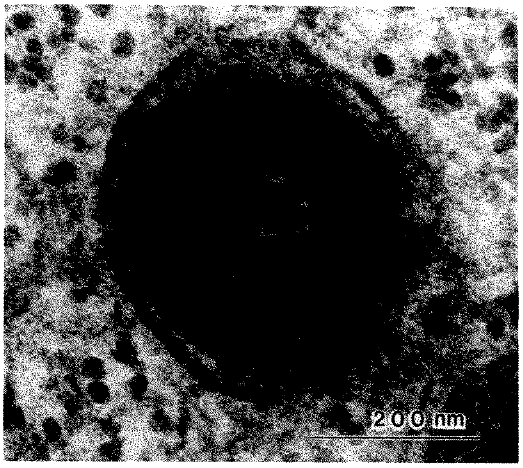

Fig 5. Immature secretory granule consisting of concentrically arranged, membranelike lamellae around less electron-dense central core (original x172,000).

freely in the lumen of the ES as well as between epithelial cells. In the perisaccular tissue, round cell nuclei not typical for fibroblasts were often seen freely located. Such nuclei could not be seen in the cadaver material or in the acoustic schwannoma material.

Epithelial cells frequently displayed dilated rough endoplasmic reticulum (rER) containing many solitary ribosomes, which were also abundant in the cytoplasm (Fig 8). Degranulation of the rER was often seen in combination with disaggregation of polyribosomes. Some clusters of free ribosomes were seen to burst out into dilated rER (Fig 8A). The amount of glycogen particles was frequently increased near rER (Fig 8C).

The number of intraepithelially located mononuclear leukocytes was increased as compared to the reference material. These cells represented lymphocytes, lymphoblasts, and monocytes. They often interacted physically with each other as well as with epithelial cells, sometimes forming rosettes (Fig 9A). Direct cytoplasmic bridges could not be seen with certainty. Macrophages containing phagocytosed material were frequently noted in the subepithelial space (Fig 9B). The labyrinthine tissue was analyzed for presence of inflammatory reaction and presence of microorganisms that could have resulted from the earlier surgical procedure. No such findings were made, even though degenerative changes in the sensory and nonsensory epithelia were frequent. These findings will be presented in a separate paper.

Ultrastructure of ES From Patients Undergoing Operations for Acoustic Schwannoma. Many of the ultrastructural changes described above were also noted in specimens obtained from patients undergoing operations for acoustic schwannoma. The lumen of the intraosseous ES often contained a considerable amount of stainable material. The density of these masses was not so pronounced. The epithelial cell nuclei were more folded and a prominent nucleolus was more frequently observed than in the cadaver material. No nuclear bodies could be seen. The endoplasmic reticulum was often vesiculated and degranulated. It contained many solitary ribosomes that floated freely inside it. The cytosol contained numerous monoribosomes that to a great extent appeared to have resulted from a disaggregation of the polyribosomes. A few binuclear cells

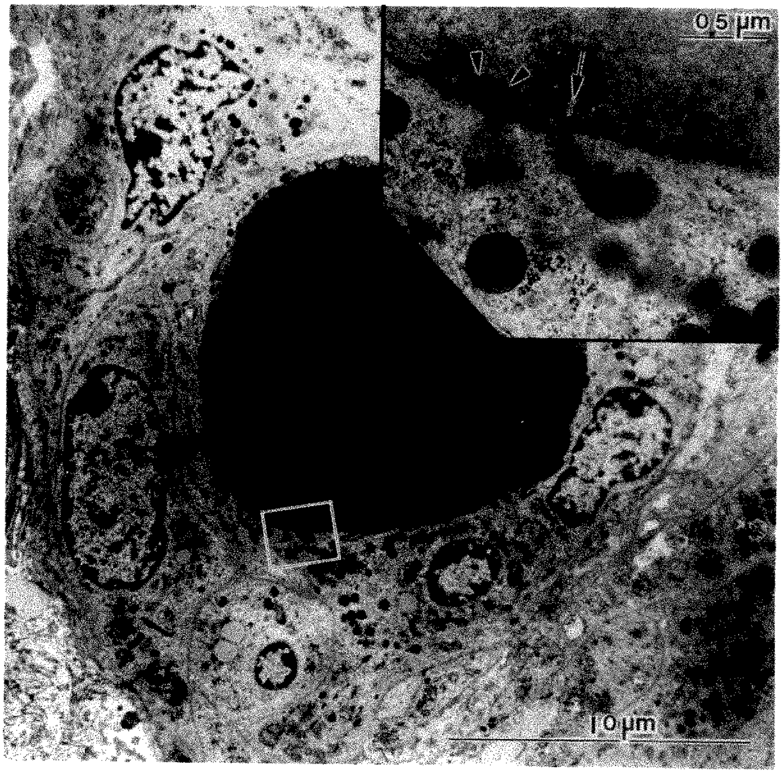

Fig 6. Epithelial tubule surrounded by cells actively involved in secretion of homogeneous substance (original x5,500). Tubule is filled with mostly homogeneous substance that shows different texture in areas with active secretion. Inset) Granules at lumen with signs of exocytosis (arrow and arrowheads). Two secretory granules show signs of exocytosis.

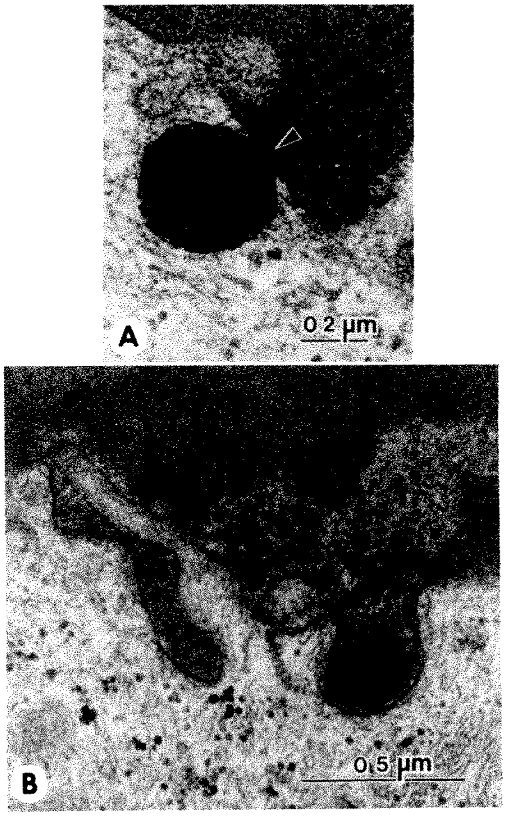

Fig 7. A) Secretory granule located close to luminal space (original x61,000). Its limiting membrane has not yet merged with apical plasmalemma (arrowhead). B) Secretory granules discharging their contents into lumen of tubule through exocytosis (original x60,000). Left granule is partly collapsed after secretion.

could be observed. Direct signs of a merocrine secretion with exocytosis of contents of membrane-bound secretory-like granules could rarely be seen. No increased accumulation of leukocytes in the epithelium could be seen. Some cells contained membrane-bound moderately dense vesicles, but it could not be assessed whether these represented primary lysosomes or secretory granules. Some epithelial cells were in a state of degeneration or had ruptured, with cell contents bursting out into the lumen of the sac.

DISCUSSION

Evidence of the relationship between histopathologic changes in the endolymphatic duct and ES and the pathogenesis of Meniere's disease is still contradictory and inconclusive. To date, only a few electron microscopic investigations of the ES have been performed, including small parts of the distal portion. Schindler et al[12] used both scanning electron microscopy and TEM to study biopsied intradural ESs of two patients with Meniere's disease. Increased deposition of collagen both inside the lumen and in the perisaccular tissue was observed, together with loss of vascularity and obliteration of the lumen.

Changes found in the ES in the present study included cell mitoses, nuclear bodies, nucleoli formation, and degranulation of rER together with a hypersecretion of glycoprotein. Degranulation of rER is a known, distinct morphologic change that is frequently accompanied by a vesiculation of the rER and disaggregation of polyribosomes. Numerous ribosomes may be lying free in the cytoplasm, and it appears as though the ribosomes have dropped off the rER into the cytoplasmic matrix. Such changes have been studied in the hepatocytes of animals subjected to various noxious influences.

Examples of dilatation and degranulation of hepatocyte rER have been seen in animals after the administration of various chemical solvents[13] and puromycin,[14] and disaggregation of polyribosomes bound to rER occurs in fibroblasts of vitamin C–deficient guinea pigs.[15]

Degranulation and disaggregation of polyribosomes may be useful morphologic indicators of depressed or altered protein synthesis. Polyribosomes comprise ribosomes attached to a fine strand of messenger RNA with encoded information that determines the amino acid sequence for the specific proteins being synthesized. The ribosomes are thought to move along the length of the messenger RNA and to be released when the specific polypeptide chain has been completed.[16] In virus-infected cells with halted cell division, disaggregation of polyribosomes also occurs, and the cytoplasm is filled with innumerable solitary ribosomes.[17]

In the present investigation many epithelial cells were found to contain prominent nucleoli and granular nucleolar bodies surrounded by an intranuclear, capsule-like structure. The nucleolus is known to be involved in the production and distribution of RNA. It is the site of synthesis of precursors of ribosomal RNA,[18] and thereby plays a key role in the protein synthesis. It may be assumed that the occurrence of prominent nucleoli in the ES epithelium is related to the high activity of secretion of a protein-rich product into the tubular structures.

Nuclear bodies have been reported to occur in several situations, including tumor formation, viral infections, hormonal and immunologic stimulation, and drug action, as well as in normal animal tissue. They probably occur universally and may be a normal constituent of the nucleus. Nuclear bodies are probably related to the nucleoli and cooperate with them in the formation of ribosomes.[19] Nuclear bodies similar to those in the epithelium of the presented specimen were not observed in the reference material. Their occurrence may be related to the high metabolic activity and protein turnover in this specimen.

The large number of cell remnants, such as cell nuclei and organelles, in the subepithelial tissue was not observed in the reference material and may therefore not represent changes caused by mechani-

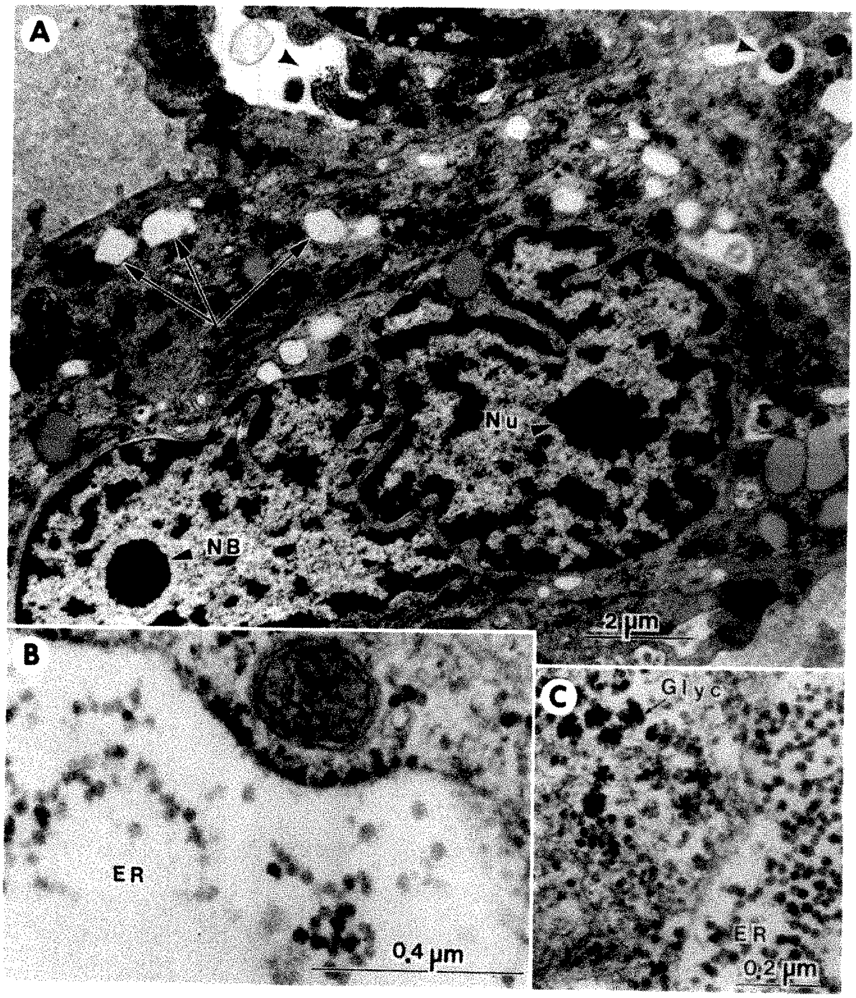

Fig 8. A) Endolymphatic sac epithelial cell with prominent nucleolus (Nu) and granular nuclear body (NB) (original x15,100). Endoplasmic reticuli are dilated (arrows) and partly degranulated. B) Endoplasmic reticulum (ER) often contains numerous solitary ribosomes (arrowheads in A) (original x109,000). C) Glycogen particles (Glyc) are seen close to dilated ER (original x78,000).

cal trauma or heating during operation. It therefore seems more likely that it is related to a pathologically increased cell turnover and cell degeneration in the epithelium of the ES. This in turn could be due to the increased metabolic rate or a direct toxic influence on the cells by some hitherto unknown factors.

Interactions of lymphocytes, lymphoblasts, and monocytes have been observed in the guinea pig ES and are believed to reflect an ongoing immunologic activity similar to that observed in antigen-challenged lymphoid tissue.[5] The presence and interactions of these cells may indicate that this ES specimen is immunologically hyperactive. Signs of viral infection could not be verified. Some viruslike structures were seen in the tubules, but their true nature could not be settled by the use of the ultrastructural technique.

Indications of the secretory capability of the human ES were, however, clear. Dense secretory granules were seen in different stages of maturation close to polyribosomes, rER, and well-developed Golgi complexes located in the juxtanuclear cytoplasm facing the apical portion of the cell. The mammalian as well as the nonmammalian ES frequently contains an eosinophilic precipitate[7,20,21] that has been believed to represent a macromolecular filtrate of endolymph accumulating after water and solute resorption.[22]

However, morphologic and experimental studies have indicated that the ES may produce and excrete its own endolymph into its lumen.[23-27] A secretion of macromolecular substances in the human ES was suspected on the basis of ultrastructural studies of cadaver material,[10] but was never proven. The normal excretory activity may be too low to see, and the secretory granules, once formed, may be so swiftly discharged during exocytosis that they escape detection.

The hypothesis was recently advanced that the ES can compensatorily secrete fluid or macromolecular complexes into the endolymphatic space when endolymph pressure is decreased.[28-31] Histochemical TEM studies of the ES in gerbils indicate a secretory pathway of glycoprotein involving both the rER and Golgi complexes.[32]

Electron microscopic, cytochemical, and autoradiographic techniques have established the role of the rER and Golgi complex in the formation and secretion of glycoprotein from the cells. Synthesis and secretion of glycoprotein conjugates seem to in-

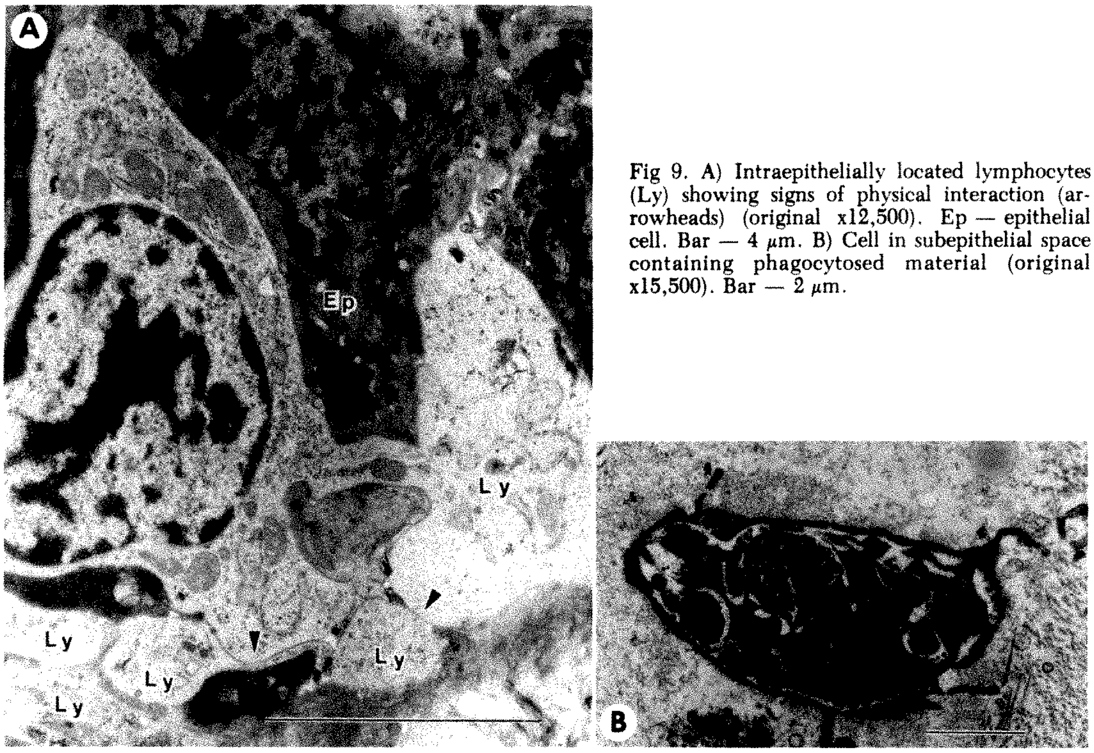

Fig 9. A) Intraepithelially located lymphocytes (Ly) showing signs of physical interaction (arrowheads) (original x12,500). Ep — epithelial cell. Bar — 4 μm. B) Cell in subepithelial space containing phagocytosed material (original x15,500). Bar — 2 μm.

volve an initial stage of protein synthesis in rER, followed by a stage of maturation into smaller secretory vesicles that are budded off from the Golgi complexes, where the carbohydrate is added to form glycoprotein.[33] However, the Golgi complex is not the sole site of uptake and coupling of sugars to proteins.

Based on our findings, the proposed pathway of intracellular secretion of glycoprotein-like material in the human ES is represented in Fig 10. Results may indicate that glycoprotein turnover is disturbed in this specimen and that this may have produced functional disturbances in the inner ear. It is possible that accumulation of fluid in the inner ear could be due to an uncontrolled, intermittent hypersecretion of glycoprotein conjugates into the sac. For such a conclusion, however, more material must be analyzed.

Alternative explanations for these changes could be a labyrinthitis or a chronic fistula between perilymph and endolymph created during the removal of the stapes, resulting in a hypersecretion of glycoprotein into the ES. Such a secretion may be observed experimentally after surgical ablation of the labyrinth. Several weeks later, after a period of phagocytosis and clearance of the glycoprotein,[8] the ES morphology is again normal. From such studies in would therefore appear more likely that the ES changes noted in this specimen are primary in nature and related to the functional disturbances in the inner ear. Theoretically, toxic, metabolic, or hormonal factors as well as viral agents could lead to a dysfunction of the ES resulting in a disturbed homeostatic equilibrium of the inner ear fluids.

This study seems to reveal the dynamic properties of the human ES epithelium. Apparently, the sac has the potential to remodel its size and shape through both epithelial tubule proliferation (Fig 11) and atrophy. This may explain why there are such great anatomic variations in this structure in different people.

Further studies of the ES, including the portion

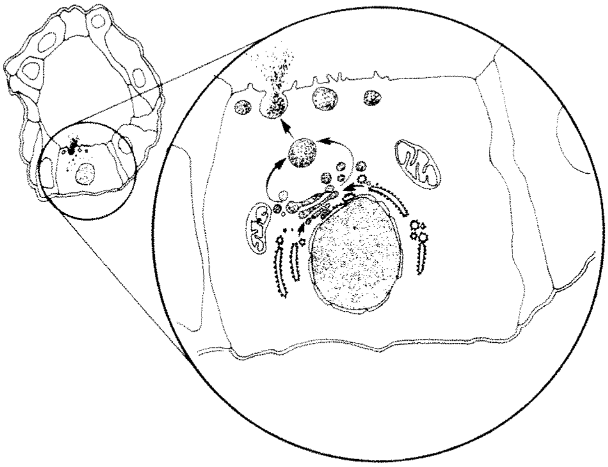

Fig 10. Schematic representation of presumed intracellular secretory pathways in epithelium of human endolymphatic sac. Synthesis and secretion of macromolecular conjugates may involve initial stage of protein synthesis in rough endoplasmic reticulum followed by stage of maturation into membrane-bound vesicles that are budded off from Golgi complex. Limiting membrane of these vesicles fuses with apical plasmalemma, leading to exocytosis.

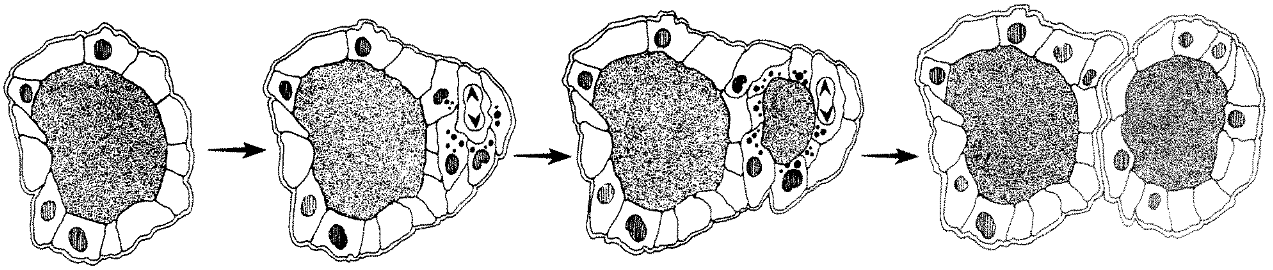

Fig 11. Hypothetical representation of events leading to hyperplastic changes of human endolymphatic sac. Epithelial cell proliferation is associated with deposition of macromolecular conjugates between adjacent cells. This may dilate intercellular space, opening up additional ramifications of epithelial tubules. Through formation of basal lamina, "new" tubule may ultimately separate from original one.

within the bony vestibular aqueduct, should provide us with more detailed information about the human ES and its possible etiologic role in Meniere's disease. Such studies are under way.

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INTERNATIONAL HEARING AID CONFERENCE: SIGNAL PROCESSING, FITTING, & EFFICACY

The International Hearing Aid Conference: Signal Processing, Fitting, & Efficacy will be held June 21-23, 1991, at The University of Iowa, Iowa City, Iowa. The organizing committee includes Richard S. Tyler, PhD (Signal Processing), Chaslav V. Pavlovic, PhD (Fitting), and Ruth A. Bentler, PhD (Efficacy). Further information may be obtained from any member of the organizing committee at the Department of Speech Pathology and Audiology, The University of Iowa, Iowa City, IA 52242; (319) 335-8726, FAX (319) 335-8851.

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TUMOR NECROSIS FACTOR ALPHA IN MIDDLE EAR CHOLESTEATOMA AND ITS EFFECT ON KERATINOCYTES IN VITRO

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NEW YORK, NEW YORK

Tumor necrosis factor alpha (TNF-α) was found in human middle ear cholesteatoma tissues by the immunoperoxidase method using rabbit anti human TNF-α immunoglobulin G. It appeared to be localized in the epithelium and connective tissue of cholesteatomas studied, particularly on basal and spinous cells, and macrophages. The epithelium of normal external ear canal skin was lightly stained, but the staining was much weaker than that of the cholesteatomas observed. In vitro, recombinant mouse TNF-α stimulated proliferation, protein synthesis, and terminal differentiation of basal keratinocytes. These stimulatory effects were blocked by the anti-TNF-α immunoglobulin G, which by itself had no effect on basal keratinocytes. These findings suggest that TNF-α plays an important role in the development of cholesteatomas seen clinically.

KEY WORDS — cholesteatoma, differentiation, keratinocyte, proliferation, tumor necrosis factor alpha.

INTRODUCTION

Tumor necrosis factor alpha (TNF-α) is a polypeptide, mainly secreted by activated macrophages, having a molecular weight of 17,000 d. It was first described as an endotoxin-induced serum factor that causes necrosis of tumor,[1] but recent studies indicated that TNF-α exerts broad activities on nonneoplastic cells. It has been reported that TNF-α plays a role in various inflammatory diseases and normal tissues. It may be an important mediator in tissue destruction and the remodeling processes by means of production of collagenase and prostaglandin E2 from various cells such as fibroblasts and synovial cells.[2] It also exhibits osteoclastic bone-resorbing activity in vitro[3,4] and the ability to destroy proteoglycan.[5] Ophir et al[6] found TNF-α in middle ear effusion and suggested that it may mediate various pathologic processes associated with otitis media. The activated macrophage is not the only cellular source of TNF-α. Mast cells,[7,8] osteoblastlike cells,[9] and keratinocytes[10] are also potential sources of TNF-α.

Cholesteatoma is a chronic middle ear disease characterized by the accumulation of keratinizing epithelium resulting from proliferation and differentiation of epithelial cells. Acquired cholesteatoma is usually associated with an inflammatory reaction, and TNF-α may be involved in the development of cholesteatoma. However, the presence of TNF in cholesteatoma has not been reported, to our knowledge. The present study was to demonstrate 1) the localization of TNF-α in human middle ear cholesteatoma tissues and 2) the effect of TNF-α on the cellular behavior of basal keratinocytes, in order to delineate the possible role of TNF in the disease process of cholesteatoma.

MATERIALS AND METHODS

IMMUNOHISTOCHEMICAL STAINING

Specimens of human middle ear cholesteatoma tissue (12) and normal external ear canal skin (6) were obtained from patients during ear operations. These specimens were fixed in 10% formaldehyde solution, and 6-μm-thick paraffin sections were made. Tissue sections were stained by the indirect immunoperoxidase method using rabbit anti human TNF-α immunoglobulin G (IgG).

In brief, the procedure of immunoperoxidase staining included the following incubation steps: first, 0.3% hydrogen peroxide, 30 minutes; then 3% normal goat serum (Cappel, Cochranville, Pa) for 1 hour; rabbit anti human TNF-α IgG (Genzyme, Boston, Mass), diluted 1:40, 30 minutes; peroxidase goat anti rabbit IgG (Cappel), diluted 1:400, 30 minutes; and 0.06%, 3,3-diaminobenzidine hydrochloride in phosphate-buffered saline (PBS) 10 minutes. In each step, tissue sections were rinsed well in PBS (four changes, each 10 minutes). The whole process was performed in a humid chamber at room temperature.

We did two control studies. One was performed with rabbit anti human TNF-α IgG, which was preincubated for 1 hour at 37°C with recombinant human TNF-α in excess to block antibody-binding sites. The other was performed by substituting PBS for rabbit anti human TNF-α IgG to determine nonspecific staining sites. The sections were then mounted with Permount and observed under a microscope.

CELL CULTURE

Epidermal basal keratinocytes were prepared from neonatal Lewis rats as described previously.[11]

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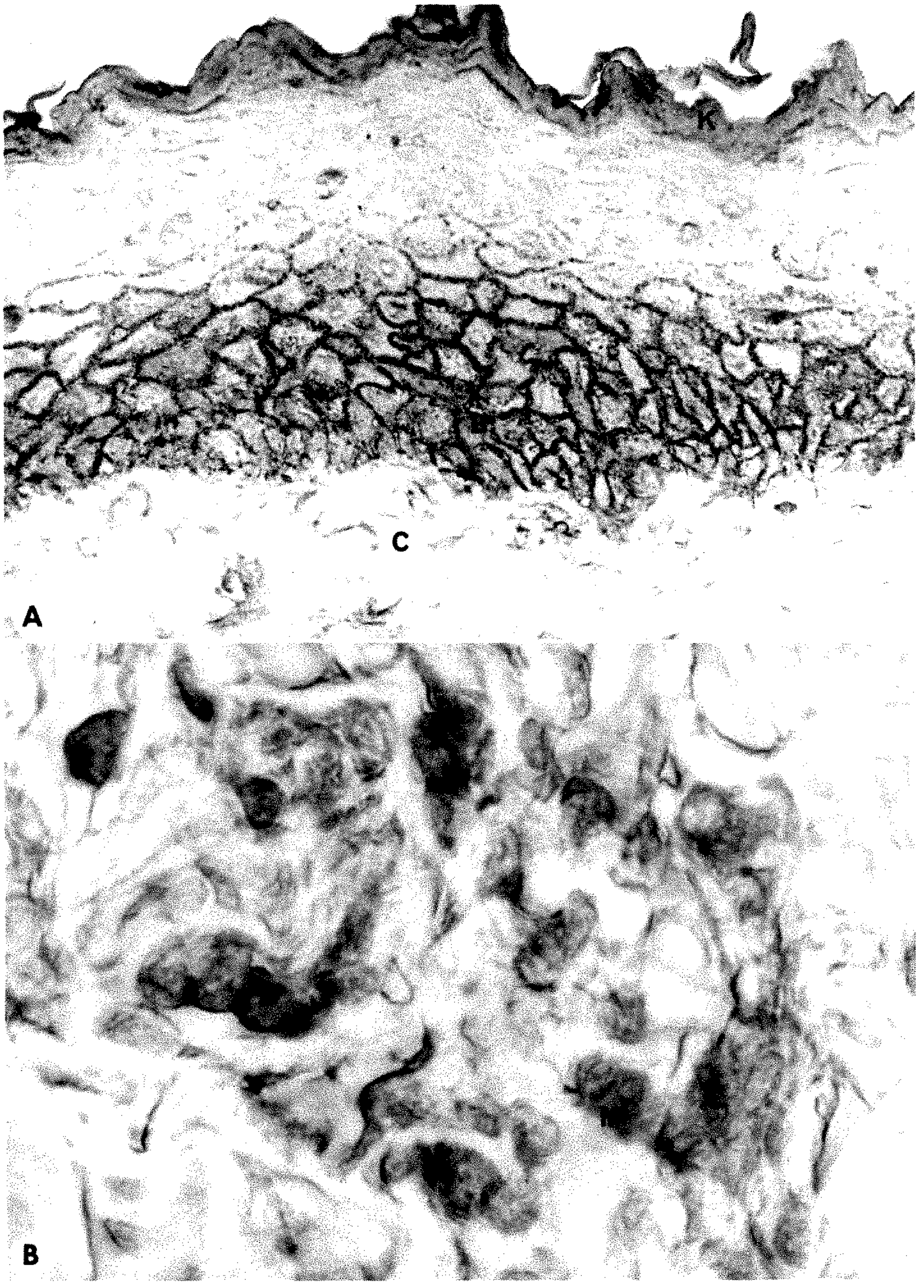

Fig 1. Immunoperoxidase staining of tumor necrosis factor alpha. A) In human cholesteatoma (original x132). Specific brownish color is noted on pericellular areas and basal cell surfaces (B). Some cells in suprabasal layer also show staining for tumor necrosis factor alpha. C — connective tissue, K — keratin. B) In subepithelial connective tissue of cholesteatoma (original x330). M — macrophages. (Continued on next page.)

The primary cells were incubated on a 24-well tissue plate (3 to 5 x 10^5 cells per well) in Ham's F-10 medium with 10% fetal bovine serum under humidification at 37°C in 95% air–5% carbon dioxide.

ASSAY METHOD

Incorporation of ^{3}H-Thymidine and ^{3}H-Histidine. Assays of proliferation and protein synthesis were performed by incorporation of ^{3}H-thymidine and ^{3}H-histidine into basal keratinocytes. When basal keratinocyte cultures neared confluence, their media were replaced by serum-free F-10 with the addition of 0 to 10 ng recombinant mouse TNF-α (Genzyme) per milliliter. The basal keratinocytes were incubated for 48 hours and then labeled with ^{3}H-thymidine or ^{3}H-histidine (0.5 μCi per well) for an additional 24-hour incubation. Incorporation of ^{3}H-thymidine and ^{3}H-histidine was determined by counting the radioactivity in cells after they were treated with 10% trichloroacetic acid and dissolved in N sodium hydroxide.

Incorporation of ^{3}H-Putrescine. Transglutaminase activity in basal keratinocytes was determined by incorporation of ^{3}H-putrescine into cells. The incorporation was performed by the addition of 0.5 μCi ^{3}H-putrescine per milliliter into the keratinocyte cultures after treatment for 48 hours with 2 ng of recombinant TNF-α per milliliter.

Isolation of Cornified Cell Envelopes. The cornified cell envelopes were formed during terminal differentiation of keratinocytes. The procedure of Cline and Rice[12] was used for isolation of the corni-

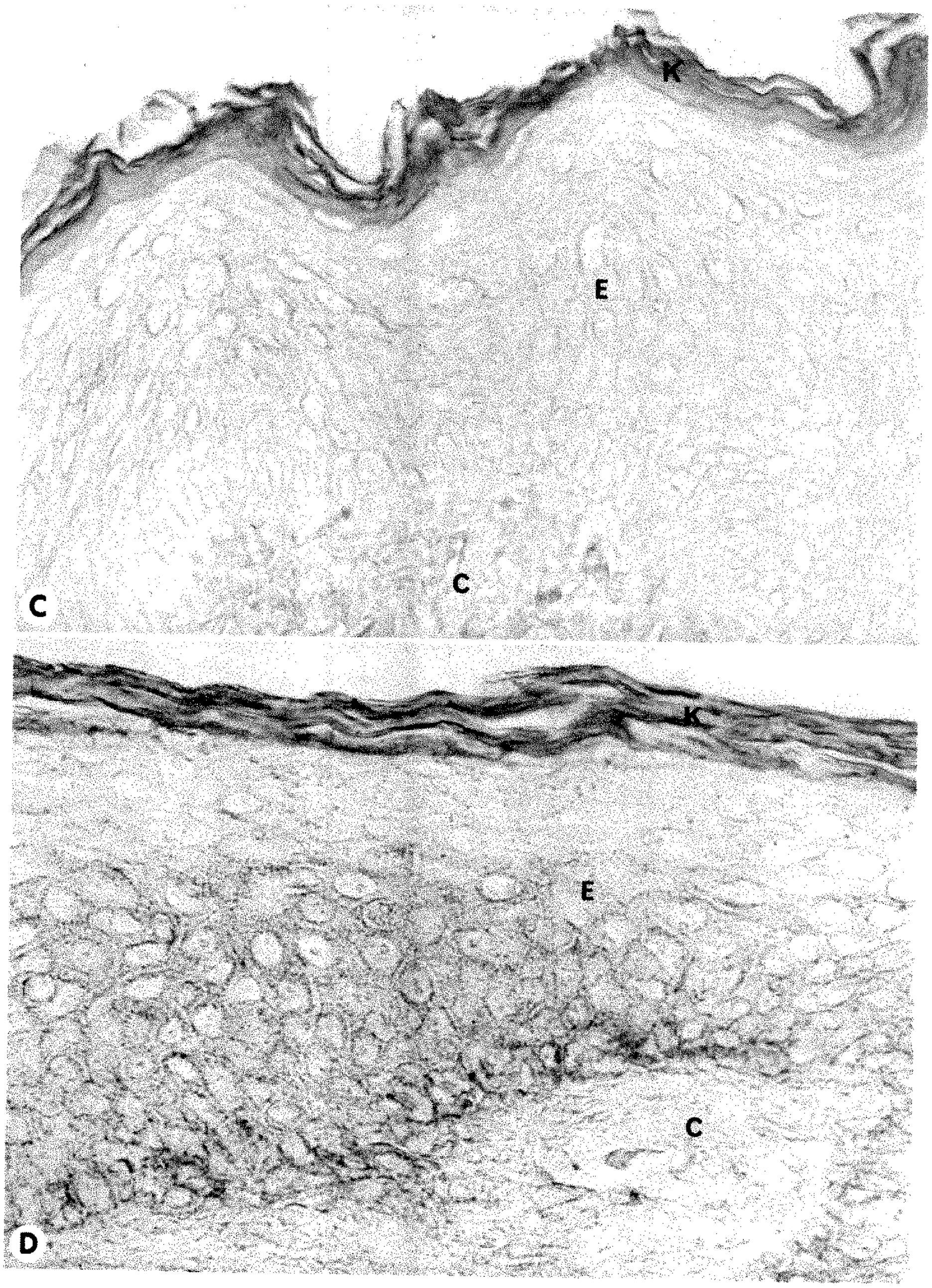

Fig 1 (continued). C) Control staining in cholesteatoma tissue (original x132). Nonspecific staining was observed in keratin area (K). E — epithelium, C — connective tissue. D) In external ear canal skin (original x132). Staining intensity is significantly weaker than that of cholesteatoma epithelium. E — epithelium, K — keratin, C — connective tissue.

fied envelopes. The keratinocytes labeled by ^{3}H-putrescine were removed from the culture plate by treatment with trypsin–ethylenediaminetetraacetic acid solution (Gibco, Grand Island, NY). The cells were collected by centrifugation at 100g for 10 minutes and resuspended in 0.5 mL serum-free F-10 medium containing 200 μmol/L of calcium ionophore A-23187 (Sigma, St Louis, Mo). After incubation at 37°C for 2 hours, cells were lysed by the addition of 50 μL of 20% (wt/vol) sodium dodecyl sulfate–20% β-mercaptoethanol at 37°C for 20 minutes. The cell envelopes were recovered by centrifugation at 10,000g for 20 minutes. Incorporation of ^{3}H-putrescine into cell envelopes and the sodium dodecyl sulfate–soluble fraction was determined by a liquid scintillation spectrophotometer.

Neutralization Experiments. Basal keratinocytes were preincubated for 1 hour at 37°C with rabbit anti mouse TNF-α IgG (50 ng/mL; Genzyme) and followed by the addition of various concentrations of TNF-α as assayed for incorporation of ^{3}H-thymidine, ^{3}H-histidine, and ^{3}H-putrescine.

RESULTS

LOCALIZATION OF TUMOR NECROSIS FACTOR ALPHA

With the immunoperoxidase staining method, TNF-α was detected as brownish color in the pericellular area and basal cell surfaces of epithelium in cholesteatoma tissues. Some cells in the suprabasal layer also showed staining of TNF-α (Fig 1A). In the subepithelial tissue of cholesteatomas, TNF-α

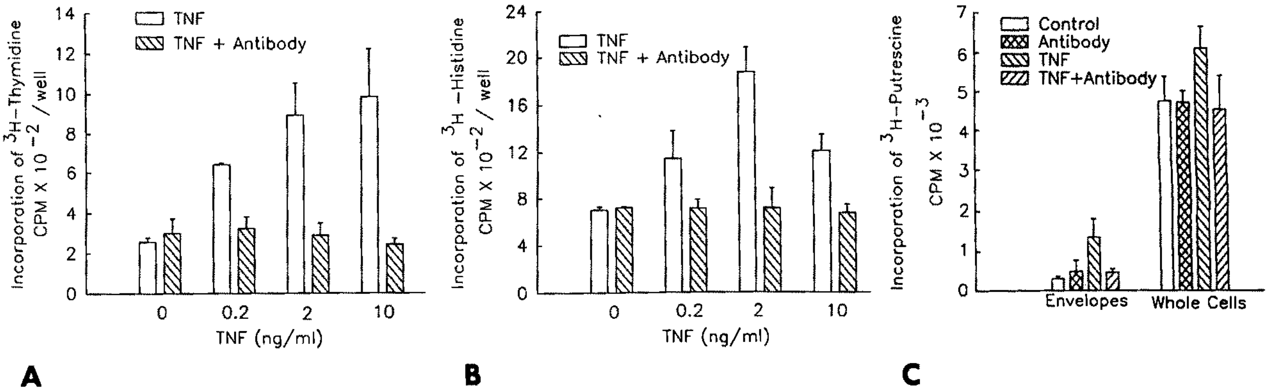

Fig 2. Effects of tumor necrosis factor alpha (TNF) (Student's *t* test, $p < .05$). Values are means of four wells of cultures ±SD. CPM — counts per minute. A) Effect on proliferation, studied by measuring incorporation of ^{3}H-thymidine into basal keratinocytes. Stimulatory effect of TNF-α can be neutralized by anti-TNF immunoglobulin G (IgG; 50 ng/mL). B) Effect on protein synthesis, studied by measuring incorporation of ^{3}H-histidine into basal keratinocytes. Anti-TNF IgG (50 ng/mL) blocked stimulatory effect of TNF on basal keratinocytes. C) Effect of TNF (2 ng/mL) on induction of transglutaminase activity, studied by measuring incorporation of ^{3}H-putrescine into cell envelopes and whole cells of keratinocytes. Anti-TNF IgG (50 ng/mL) neutralizes effect of TNF on keratinocytes.

was noted on macrophages and mononuclear cells (Fig 1B). The staining of keratin debris was nonspecific, as demonstrated by the control staining, in which the primary antibody was absorbed with antigen, eg, human TNF-α (Fig 1C) or replaced by PBS (data not shown).

There was no staining of TNF-α in epithelium and subepithelial connective tissue in the control study when the rabbit anti human TNF-α antibody was blocked by antigen human TNF-α (Fig 1C). This is an essential negative control, because the only direct way to establish specificity in immunohistochemical staining is to inhibit that staining by addition of the antigen to a working solution of the antibody.[13] This is also the only way to know what antigen is localized in a given immunohistochemical staining.[13] Thus, the fact that immunohistochemical staining is able to be blocked by absorption of anti-human TNF-α antibody with its antigen human TNF-α shows that the reaction is indeed specific.

In normal external ear canal skin, the squamous epithelium was lightly stained, but much more weakly than that of the cholesteatomas (Fig 1D).

IN VITRO STUDIES

The effect of TNF-α on proliferation was determined by the incorporation of ^{3}H-thymidine into basal keratinocytes in the presence of different concentrations of TNF-α. Figure 2A shows that TNF-α stimulated the growth of basal keratinocytes in a dose-dependent manner. There was no effect of anti–TNF-α IgG on the growth of basal keratinocytes; however, the stimulatory effect of TNF-α was abrogated by anti–TNF-α IgG antibody.

The effect of TNF-α on the protein synthesis was studied by measuring the incorporation of ^{3}H-histidine into keratinocytes. As shown in Fig 2B, TNF-α stimulated the protein synthesis by increasing incorporation of ^{3}H-histidine with the optimal concentration of 2 ng/mL. Again, this stimulatory effect of TNF-α was neutralized by the addition of anti–TNF-α IgG.

We also studied the effect of TNF-α on the terminal differentiation of basal keratinocytes, during which the cell envelopes were seen to form beneath the plasma membranes. These envelopes consist of highly insoluble protein resulting from the formation of the γ-glutamyl-ϵ-lysine isopeptide cross-linkage by the action of transglutaminase.[14] The effect of TNF-α on the transglutaminase activity was studied by measuring the incorporation of ^{3}H-putrescine into cell envelopes and cells.[15] We found that TNF-α significantly stimulated the incorporation of ^{3}H-putrescine into cell envelopes and cells. Anti–TNF-α IgG entirely neutralized this stimulatory effect. This increase in incorporation of ^{3}H-putrescine implies that TNF-α stimulates transglutaminase activity when basal keratinocytes undergo terminal differentiation (Fig 2B).

DISCUSSION

The development of acquired cholesteatoma is due to proliferation and differentiation of epidermal basal cells in response to the inflammatory reaction in the middle ear cavity. In the present study, TNF-α appeared to be localized in the epithelium and granulation tissue of the cholesteatomas. Since the granulation tissue of a cholesteatoma contains macrophages and mononuclear cells, the TNF-α in the epithelium of a cholesteatoma may be derived from macrophages or mast cells.[7,8] On the other hand, the epithelial cells activated by inflammation may have the capacity to produce their own TNF-α. Unstimulated epithelial cells do not produce a remarkable level of TNF-α, as shown by the weak staining of normal external ear canal skin.

Since activated keratinocytes are capable of producing their own TNF-α,[10] this cytokine may serve as an autocrine growth regulator. Our present in vitro studies showed that TNF-α stimulated proliferation, protein synthesis, and terminal differentiation of keratinocytes. This action enhances keratin debris production. The keratin debris may act as an inflammatory stimulus to form granulation tissue. Moreover, the accumulation of keratin debris may lead to an increase in the size and destructiveness of a cholesteatoma under clinical conditions. However, it seems to be contradictory that TNF-α stimulates both proliferation and terminal differentiation of keratinocytes. In vivo, the basal keratinocytes in cholesteatomatous epithelium, as in normal skin epidermis, are in a process of homeostatic balance, during which undifferentiated cells multiply in the basal layer, with some cells leaving the basal layer to begin terminal differentiation.[16] The mechanism of this homeostatic balance between proliferation and terminal differentiation of basal keratinocytes in vivo is still not well defined. Further study is required to elucidate this process.

In conclusion, the combined evidence of immunohistochemistry, showing the presence of TNF-α in the cholesteatoma tissue, and in vitro studies, demonstrating proliferative activity in the keratinocyte, suggests that TNF-α may be involved in the development of cholesteatoma.

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IMAGING CASE STUDY OF THE MONTH

SPHENOID SINUS METASTASIS DISPLACING THE CAVERNOUS SINUS

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JAMES A. KENNEY, JR
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The following case is presented to illustrate the effect of a sphenoid sinus metastasis upon vision, oculomotor function, and the cavernous sinus.

CASE REPORT

The patient was a 70-year-old man who at the age of 3 had had a traumatic loss of the left eye. In mid-September 1988 he started seeing "weaving lines" on the temporal side of the right visual field with blurred vision. By the end of September, an ophthalmologist estimated his visual acuity as 20/100 and discovered a small mass in the inferior right eyelid. The ophthalmologist thought it was a chalazion and prescribed topical treatment. During the first week of October, the patient's vision progressively decreased and he became blind. He also had paralysis of all the external ocular muscles. On October 12, 1988, the small mass was removed. Unexpectedly, the pathology report described a "sebaceous carcinoma with epidermoid transdifferentiation." The patient was then referred to The University of Iowa Hospitals and Clinics.

At admission on October 17, 1988, he was found to be cachectic and dehydrated. The globe of the right eye was resistant to retropulsion. There was no chemosis, proptosis, or periorbital edema. The eyelid was drooping and the pupil was dilated to 6 mm and unreactive to light. The external ocular movements were only 5% to 10% in all directions. The fundus showed a pink disc with minimal or modest inferotemporal pallor. There was decreased sensation along the V-1 distribution; V-2 and V-3 were intact, as were the other cranial nerves. The right eyelid was swollen and ulcerated, with yellowish fluid draining from it. The conjunctiva was injected. The rest of the findings on physical examination were unremarkable. A differential diagnosis of cavernous sinus thrombosis, lymphoma, Wegener's granulomatosis, mucormycosis, or aspergillosis was made.

On October 18, 1988, the patient underwent a right-sided sphenoidotomy and biopsy. Pus was not present in the cavity. The mucosa was thickened and hypertrophic. Histologic study revealed poorly differentiated epidermoidal carcinoma similar to the sebaceous carcinoma removed from the eyelid. Radiotherapy of the lesion was then recommended. Follow-up 1 year later demonstrated no progression of symptoms.

RADIOGRAPHIC FINDINGS

An enhanced axial computed tomography (CT) examination of the head showed a right-sided parasphenoid mass with a low-density center and an enhanced margin (Fig 1A). The superior orbital vein was normal in size. A bone window view of the same CT slice revealed complete opacity of the right sphenoid sinus (Fig 1B). Both modalities showed a left ocular prosthesis.

Direct coronal CT views of the sphenoid sinus were also obtained. A view in the plane of the midsella using a soft tissue window (Fig 2A) showed the right low-density parasellar mass. The mass displaced the cavernous sinus laterally and elevated the adjacent carotid artery. Another soft tissue window view made 8 mm posterior to the previous view showed elevation of the posterior clinoid process by the parasphenoid mass (Fig 2B). Complete opacity of the sphenoid sinus was present. A bone window view of this CT slice demonstrated erosion of the right lateral sphenoid sinus wall adjacent to the superior orbital fissure (Fig 2C).

DISCUSSION

Sebaceous gland carcinomas are rare tumors arising almost exclusively from the skin of the eyelids. The most common sites are the meibomian glands and the sebaceous glands of Zeis. Less often the site of origin is in the caruncle or the skin of the eyebrow. Clinically the lesion presents as a small hard nodule with a rubbery consistency like an atypical or recurrent chalazion. It shows a tendency to invade the overlying epithelium in a pagetoid manner, forming nests of cells that may completely replace the entire thickness of the epithelium (intraepithelial carcinoma), and clinically appears as a

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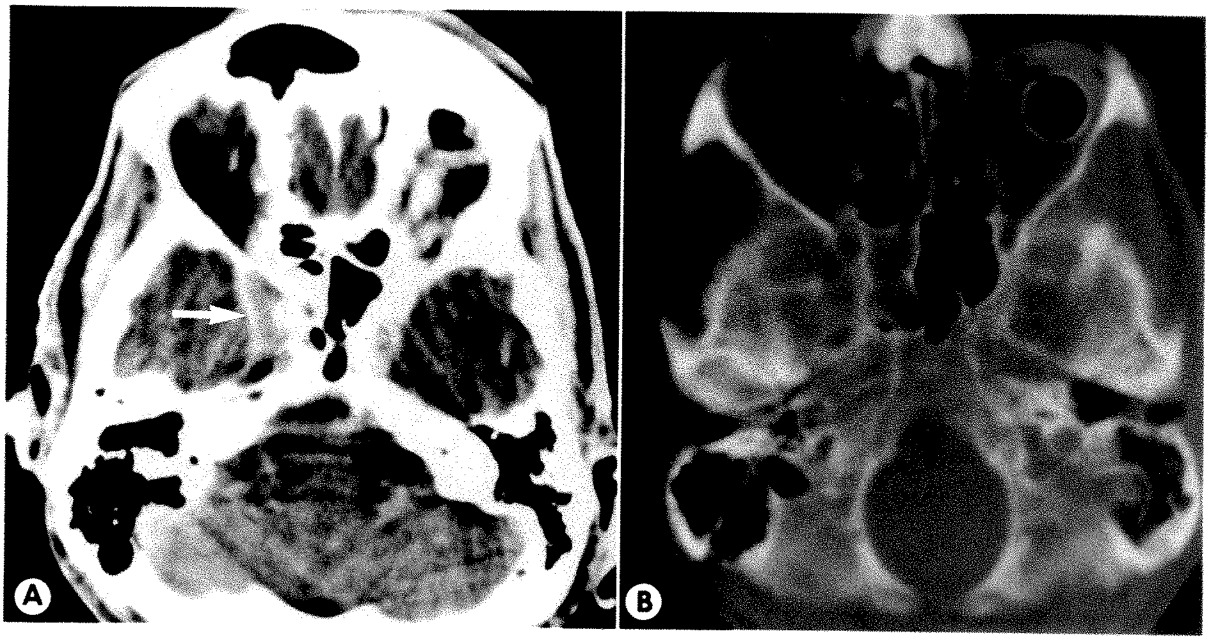

Fig 1. Axial computed tomograms. A) Soft tissue window through lower sphenoid plane with enlargement of right cavernous sinus (arrow). B) Bone mode window through same plane showing opaque right sphenoid sinus and left ocular prosthesis.

diffuse plaquelike thickening. This tumor presents four histologic patterns: nodular, comedocarcinoma, papillary, and mixed. The tumor may also show various grades of differentiation, from well to poorly differentiated. The highest grade has a tendency to perineural invasion and invasion of the lymphatic channels.

Rao et al[1] reported on 104 patients with sebaceous gland carcinoma. In approximately 20% of the patients, the orbit was directly invaded by tumor, and 23% had enlarged nodes in the preauricular or cervical area. In some cases, the primary tumor was relatively small, with a very large preauricular node. The tumors may metastasize to the lungs, liver, brain, or skull.[1]

Unfavorable prognostic factors are site of origin in the upper lid, a primary tumor greater than 10 mm in diameter, symptoms of more than 6 months' duration, an infiltrative growth pattern, and high-grade invasion of local structures, including the orbit, vessels, and lymphatic channels.

Sphenoid sinus tumors are rare, as demonstrated by the paucity of information available in the literature. Primary carcinoma of the sinuses as well as metastatic carcinoma to the sinuses most often involves the maxilla, ethmoid sinus, sphenoid sinus, and frontal sinus, in descending order.[2] Sphenoid sinus tumors comprise fewer than 1% of all sinus malignancies.[3] Carcinomas of the sphenoid sinus may start in the sphenoid or represent extension from the ethmoid sinus, maxillary sinus, or nasopharynx.[4] Carcinoma of the sphenoid sinus commonly penetrates the sella or lateral walls and roof of the sinus; therefore, the neurovascular structures adjacent to the sphenoid sinus are at risk of damage by extramucosal extension. The abducens nerve is paralyzed more frequently than any other cranial nerves supplying the extraocular muscles. Although the sphenoid sinus has a low incidence of malignant disorder, it is the most commonly involved sinus when cranial neuropathy is present.[5] Sinus carcinomas invade the cranial nerve perineural sheath.[6] This decreases the probability of surgical cure, but radiotherapy may arrest the progress of the lesion.

Tumors of the head and neck can involve the cavernous sinus by destroying the basisphenoid or by extension through the foramina at the base of the skull by spreading along the blood vessels and spreading intracranially along the peripheral nerves.[7,8] A pathologic cavernous sinus process produces incomplete or complete ophthalmoplegia that is usually painful and is commonly associated with deficits in the first or second division of the trigeminal nerve.[9] The added finding of visual loss further localizes the lesion to the anterior cavernous sinus and orbital apex. Metastases to the sphenoid sinus commonly cause an acute, painful, rapidly progressive ophthalmoplegia. In patients with this symptom the use of high-resolution CT is crucial to the diagnosis of cavernous sinus metastasis, since it can confirm the presence of a mass.[10]

Computed tomography may reveal a change in size, density, or configuration indicative of cavernous sinus abnormality. Contour bulging is the most sensitive indicator of cavernous sinus disease. Contrast enhancement is essential for evaluation of the cavernous sinus.[11,12] Chung et al[13] emphasized the need for both axial and coronal CT projections in the study of the cavernous sinus.

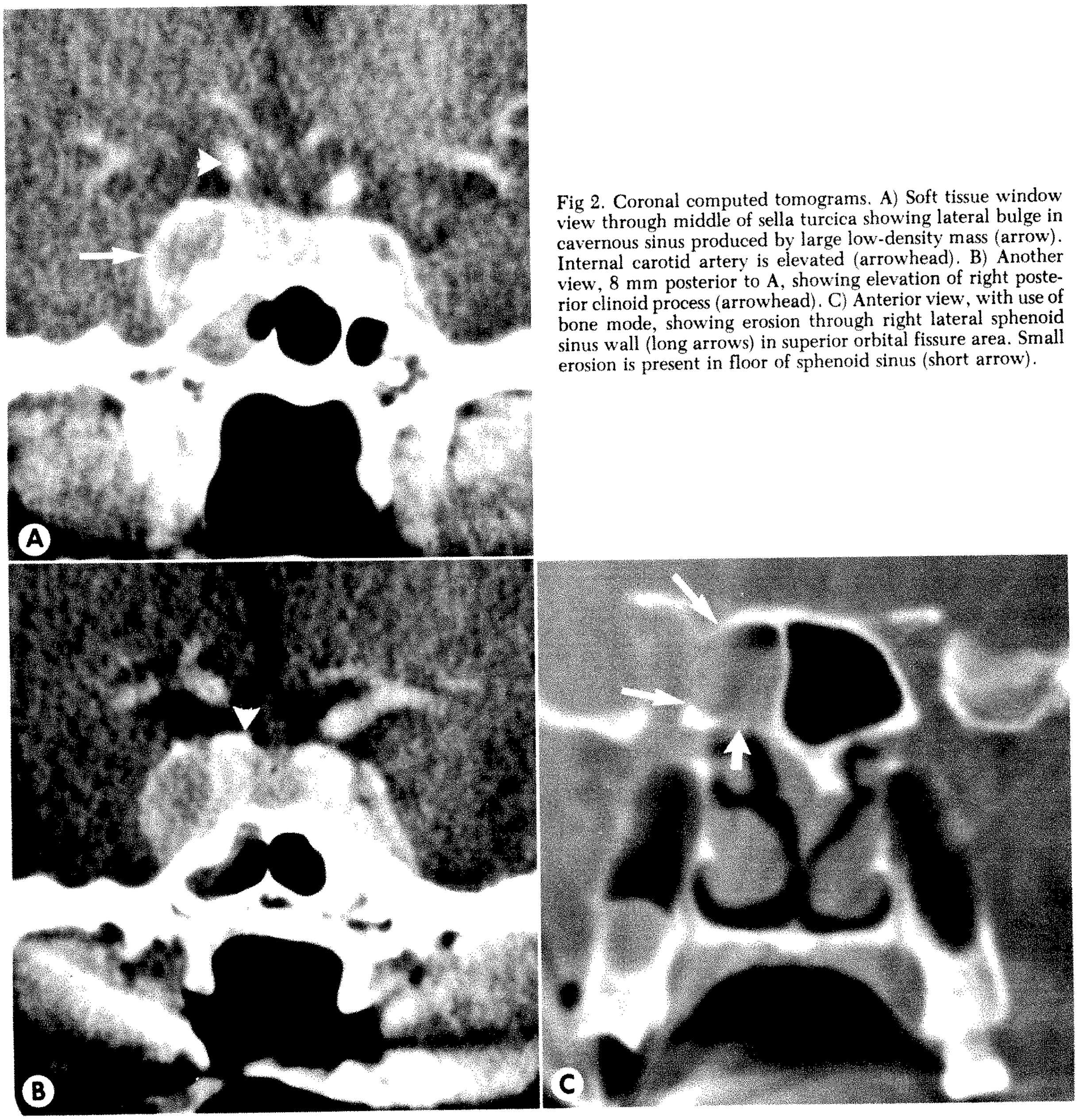

Fig 2. Coronal computed tomograms. A) Soft tissue window view through middle of sella turcica showing lateral bulge in cavernous sinus produced by large low-density mass (arrow). Internal carotid artery is elevated (arrowhead). B) Another view, 8 mm posterior to A, showing elevation of right posterior clinoid process (arrowhead). C) Anterior view, with use of bone mode, showing erosion through right lateral sphenoid sinus wall (long arrows) in superior orbital fissure area. Small erosion is present in floor of sphenoid sinus (short arrow).

Our patient represents a case in which an unusual sebaceous gland tumor spread from the lid area, presumably by a venous route, to the sphenoid sinus, where the tumor enlarged and eroded through the lateral sinus wall into the orbital apex. Oculomotor and ophthalmic nerve involvement produced ophthalmoplegia and visual loss. The lesion also invaded the cavernous sinus, producing bulging, posterior clinoid elevation, and carotid artery displacement. The cavernous sinus was not completely obstructed, as evidenced by a lack of dilatation of the superior ophthalmic vein.

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PATHOLOGY CONSULTATION

GRANULOMATOUS SIALADENITIS

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Granulomatous inflammation in salivary tissues is most often a response to liberated ductal contents, particularly mucin, in various degrees of obstructive sialadenopathy. Far less often is a granulomatous sialadenitis the result of specific infective granulomas or systemic granuloma-forming diseases. In these instances, the salivary parenchymal involvement is usually secondary to disease localization in regional lymph nodes.

Granulomatous inflammation is heterogeneous with regard to its pathogenesis, cellular composition, and intensity.[1] Evolution of the inflammation, in turn, depends on the nature of the provoking agent, its degradability, and whether or not there is an immunologic component.[2]

Despite intensive study of the cellular and molecular biology of granulomatous inflammation, the cause of many forms of granulomatous disease, eg, sarcoidosis, remains unknown. As a result, there is an imperfect division of the inflammation into two broad categories: a hypersensitivity type and a foreign body type that does not appear to involve an antigen-specific reaction.[1] These generalities apply equally to salivary and nonsalivary granulomatous inflammation. At any site the tissue reaction is a localized or diffuse collection of macrophages, epithelioid cells, lymphoid cells, and multinucleate (Langhans' or foreign body) giant cells. Epithelioid granulomas of a sarcoidal or mycobacterial type and necrosis need not be present in all forms of granulomatous inflammation.[3]

The Table is a listing of various forms of granulomatous sialadenitis. An obstructive sialadenopathy with rupture of ducts and leakage of ductal contents (Fig 1), particularly mucin, is the most common cause for a granulomatous sialadenitis in either major or minor salivary glands.[4] The labial mucocele is the best-known representative of this group. It, however, is rarely populated with epithelioid granulomas. A mucocelelike inflammatory reaction is also seen in duct obstructions or ruptured mucin-rich neoplasms in the major salivary glands. Discrete, nonnecrotic, epithelioid granulomas close to degenerating ducts are also found in obstructive sialadenopathy of major salivary glands, especially in the submandibular gland.[5]

Granulomatous sialadenitis produced by specific infective agents is certainly not common and is most often secondary to regional lymph node involvement. Parenchymal rather than nodal granulomatous inflammation characterizes the rarely occurring salivary manifestations of noninfective granulomatous diseases such as Wegener's granulomatosis[6] and Crohn's disease.[7] Salivary granulomas of sarcoidosis may be parenchymal, intranodal, or both.

The granulomatous tissue reaction related to primary salivary gland tumors can be very destructive because of the tissue toxicity of their contents. The lipid-rich Warthin's tumor can provoke an extensive foreign body necrosis leading to fistula formation (Fig 2). The pericystic foreign body reaction to the secretory products of an acinic cell carcinoma can be almost pathognomonic of that carcinoma. These necrotizing reactions contrast with the epithelioid granulomas sometimes seen in relation to the epimyoepithelial islands in lymphoepithelial lesions.

Mycobacterial (tuberculous or nontuberculous)

GRANULOMATOUS SIALADENITIS

- Obstructive sialadenopathy
  - Mucoceles
  - Extravasated mucin or secretory products
- Specific infections
  - Mycobacterial (tuberculous and nontuberculous)
  - Cat-scratch disease
  - Tularemia
  - Fungal
  - Toxoplasmosis
  - Other
- Sarcoidosis
- Associated with extrasalivary systemic disease
  - Wegener's granulomatosis
  - Crohn's disease
  - Other
- Associated with salivary tumors
  - Acinic cell carcinoma
  - Mucoepidermoid carcinoma
  - Warthin's tumor
  - Lymphoepithelial lesion
- Foreign body granulomas and iatrogenic, eg, sialography

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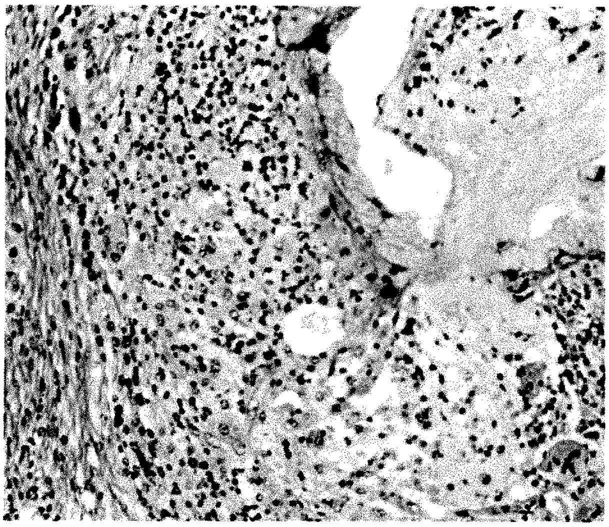

Fig 1. Rupture of interlobular duct in submandibular gland with extravasation of mucin into periductal tissues (H & E, original x180). Granulomatous reaction to mucin is early in development, but does manifest giant cells.

disease affecting the major salivary glands is rare even in countries in which the disease is prevalent.[3,8,9] The involvement of the glands is usually unilateral and is almost never primary in the parenchyma, but rather in parotid or submandibular gland lymph nodes — the former more often than the latter. Sublingual and minor salivary gland involvement is also unusual and in nearly every instance is secondary by a contiguous extension. Subjects of any age can be affected, but disease in infants is exceptional. There need not be histologic or clinical evidence of extrasalivary tuberculosis, although it should be noted that human immunodeficiency virus fosters reactivation of a latent tuberculosis.[10]

The range of histologic lesions in either form of mycobacterial disease depends on the immune state of the host. With a high-order immunity, there are nonnecrotic epithelioid cell granulomas — so-called "hard" tubercles with no detectable bacilli. In low-order immunity states, there are numerous bacilli and necrosis — so-called "soft" tubercles. The more readily recognized necrotic epithelioid cell granulomas with some bacilli are in the middle of the spectrum (Fig 3).

"The diagnosis of sarcoidosis is established by the presence of characteristic granulomas without caseation in a patient with clinical findings and symptoms consistent with the disease in whom specific granulomatous infection can be excluded by culture or immunologic testing." This quotation from McCaffrey and McDonald[11] defines how surgical pathologists should approach sarcoidosis in general and sarcoidal granulomas in salivary tissues in specific. Little help is derived from the reported wide range of clinical involvement of the major salivary glands, preponderantly the parotid — with or without Heerfordt's syndrome. Greenberg et al[12] reported an incidence of 6% in patients with histologically confirmed, generalized sarcoidosis. Miglets et al[13] claim parotid gland sarcoidosis is clinically transient and self-limited in about 40% of patients with known generalized sarcoidosis. Others, using uptake techniques, place the clinical involvement of the parotid gland as high as 75%.[14] Proven and histopathologic evidence of sarcoid in minor salivary tissues is less ambiguous (50% to 58%), as evinced by lower lip biopsies.[14,15]

In contrast to the mycobacterial granulomas, those of sarcoid in the salivary glands are less often confined to lymph nodes and may be exclusively parenchymal, particularly in interlobular and intralobular septae. The granulomas are of the "hard" variety, but may exhibit fibrinoid necrosis and often become confluent (Fig 4).

Necrotizing granulomatous inflammation is the

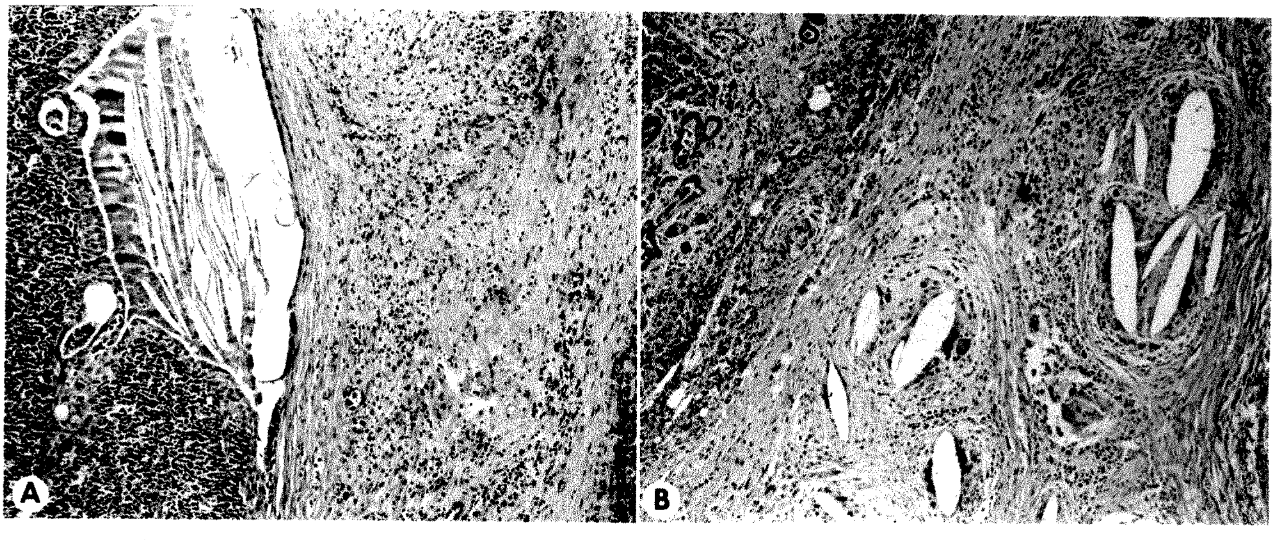

Fig 2. Warthin's tumor of parotid gland (H & E, original x80). A) Lipid-rich secretory product in attenuated duct. B) Extensive foreign body-type granulomatous reaction to ruptured tumor.

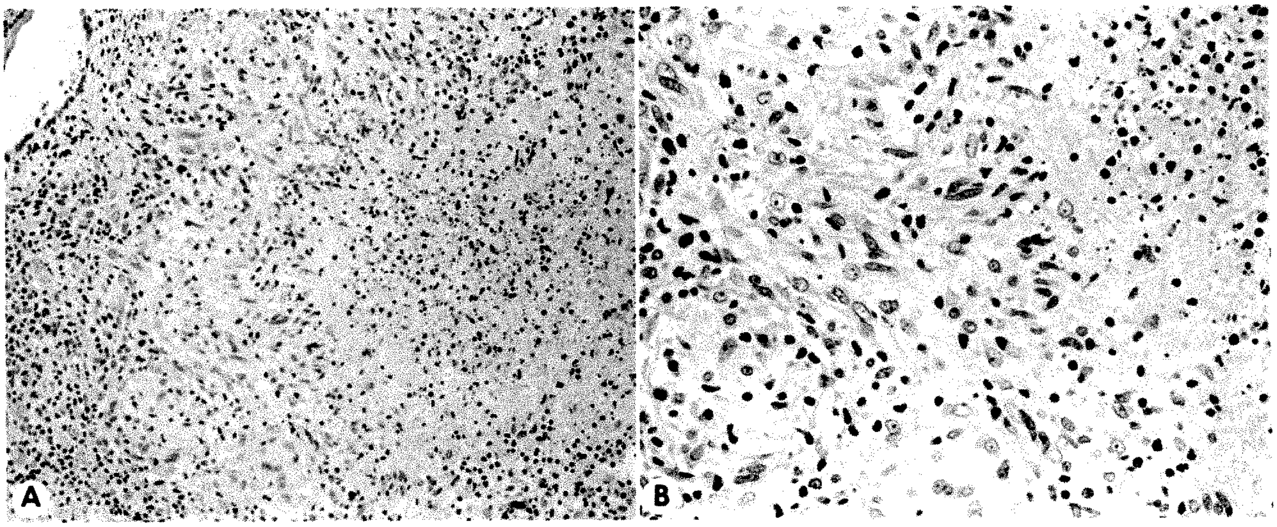

Fig 3. Parotid lymph node with tuberculous lymphadenitis. A) Palisading epithelioid cells and microgranulomas surround necrotic center of granuloma (H & E, original x80). B) Focus of granulomatous inflammation in lesion (H & E, original x180). Necrosis (upper right) is accompanied by epithelioid cells and giant cells.

histologic hallmark of tularemia, cat-scratch disease, and Wegener's granulomatosis. Extrasalivary clinical and histologic manifestations are always present. Salivary gland involvement is secondary to regional lymph node granulomas in tularemia and cat-scratch disease, while the parenchymal involvement by Wegener's granulomatosis is part of that disease's systemic spread.

A sizable proportion of the signs and symptoms of tularemia present in the head and neck, especially in endemic areas. In a Finnish study of 1,100 patients with tularemia, 12% had their main clinical manifestations in the head and neck.[16] Cervical or auriculoparotidean lymphadenopathy or abscesses were the most common findings. Spread from these nodal areas to the major salivary glands produces a granulomatous sialadenitis.

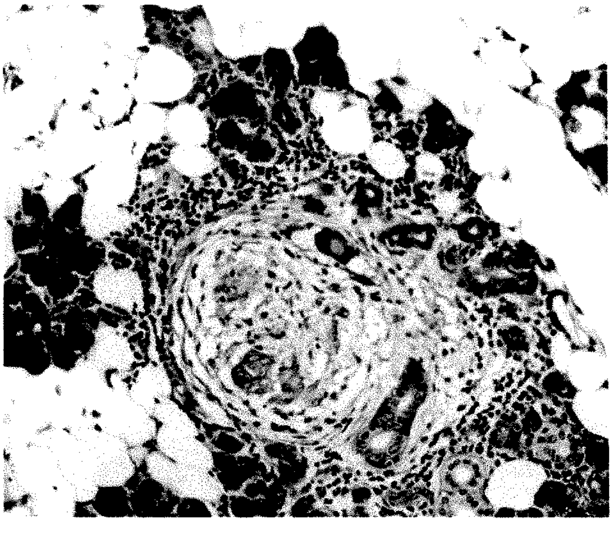

Fig 4. Sarcoid granuloma in parotid gland (H & E, original x120). Patient had clinically evident pulmonary sarcoidosis.

An even larger percent (50%) of patients with cat-scratch disease will present with a head and neck mass produced by a granulomatous inflammation provoked by an extracellular, pleomorphic, gram-negative, non-acid-fast bacillus stainable with Warthin-Starry silver stains.[17,18] The lesional tissue is first intranodal and not parenchymal in salivary regions.[19] Tularemic granulomatous inflammation often has its three evolutionary stages coexisting so that lymphoid hyperplasia, granuloma formation, and microabscesses and macroabscesses can be seen in affected tissues.

Cats also play important roles in the transmission chain of toxoplasmosis, a well-recognized specific cause of lymph node enlargement that may involve the lymph nodes associated with the major salivary glands.[20,21] Histologic diagnosis of lymph node toxoplasmosis is based on the changes in the lymph node and not on the specific demonstration of the organism itself.[22] The general nodal structure is preserved and is reactive. Small groups of epithelioid-like cells with abundant pale eosinophilic cytoplasm, seen both in the paracortical area and germinal centers, are characteristic. Clusters or strands of the cells may be the pattern in paracortical areas. Rarely, larger granulomalike groupings of cells with Langhans' type giant cells are seen. Sarcoid-like granulomas are foreign to the diagnosis.[22] Lymph nodes with small groups of epithelioid cells but with a disturbed overall nodal architecture and absence of germinal centers require careful study to exclude non-*Toxoplasma* lymphomas.[22]

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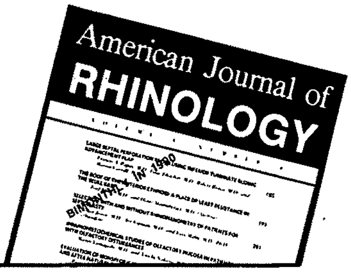

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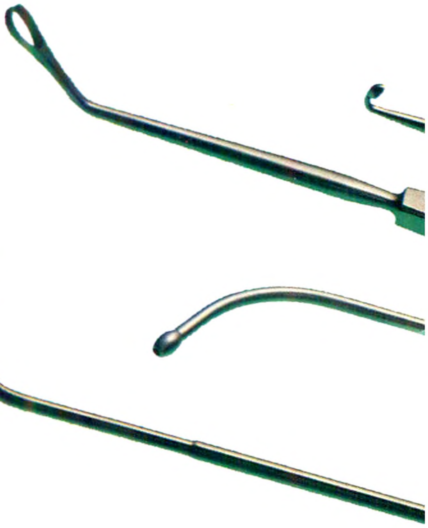

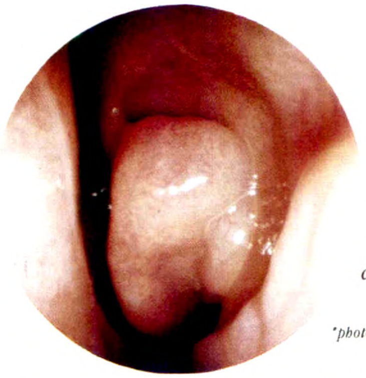

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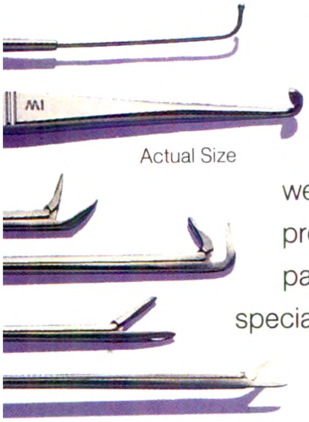

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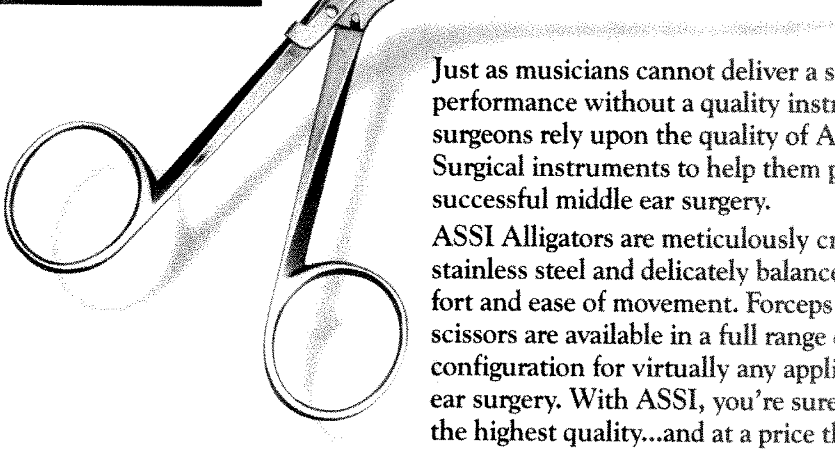

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HISTOLOGIC EVALUATION OF THE LARYNX IN SUDDEN INFANT DEATH SYNDROME

DONALD F. N. HARRISON, MD, PHD
HORLEY, ENGLAND

Seventy-four larynges removed at death from children who died of sudden infant death syndrome (SIDS) have been studied by serial sectioning in the transverse plane. An increase in subepithelial glandular tissue is seen in many specimens, and the reduction in the available subglottic area has been measured with the Measuremouse Image Intensifying system. This preliminary report confirms that in some of these children with SIDS, particularly around the age of 3 months, there is a potentially lethal reduction in subglottic airway secondary to an increase in mucus-secreting glands, possibly from an associated mild upper respiratory tract infection. Accepting that adequate control infants within this age group who have not had any trauma to the laryngotracheal area are not available, these findings offer a possible explanation for what are always tragic events.

KEY WORDS — histology, larynx, sudden infant death syndrome.

As infant mortality diminished in the first half of this century, more attention began to be given to those infants dying unexpectedly. The skills required to study these tragedies have not, however, been developed, and diagnosis varies from "pneumonitis" to "suffocation." Within the United Kingdom the term "cot death" and in the United States "sudden infant death syndrome (SIDS)" have been coined to cover "the sudden death of any infant or young child, which is unexpected by history and in which a thorough postmortem examination fails to demonstrate an adequate cause of death." It is now the commonest cause of death between 28 days and 12 months in the Western Hemisphere, accounting for at least two fifths of all postneonatal deaths. Unfortunately, SIDS is not itself a diagnosis, but rather a label covering a multitude of causes — and one or two sins!

Virtually no episodes occur among infants less than 1 week of age, and SIDS increases in frequency with each successive week, reaching a peak at 3 months, then gradually decreasing. Geography is no barrier to SIDS, although there is a disparity in incidence, varying from 1.5 to 3.5 per 1,000 live births in Europe and the United States, but dropping to around 0.19 per 1,000 live births in Hong Kong, where crowded conditions may confer an advantage, for infants are rarely left alone.

A number of common factors may offer guidance as to possible causes. Two thirds of deaths occur between noon and midnight, usually during the colder months. Eighty-eight percent of victims are said to be found in a prone position.[1] Many have evidence of a mild nonbacterial upper respiratory tract infection, with intrathoracic petechiae seen at postmortem in 80% of cases. This has been explained as indicative of terminal upper airway obstruction, and efforts have been made to associate SIDS with unsuspected obstructive sleep apnea.

Although there is some evidence that low-birth weight infants are at a higher risk of SIDS, this risk has not been confirmed in larger studies. There is, however, a male preponderance. Davies[2] has comprehensively covered many of the theories advanced to explain this family disaster. Unhappily, the plethora of hypotheses has created more confusion than enlightenment, for the value of any theory has to be measured by its compatibility with generally accepted facts. Death is sudden, and in most cases the infant is dead when first discovered. Consequently, the duration of potentially recognizable symptoms is unknown but unlikely to be longer than a few hours. Death in SIDS is silent, and signs of struggle (except possibly in infanticide) are frequently absent.

Although not numerically frequent, sudden deaths of apparently healthy infants are a national disaster. The psychological impact, coupled with permanent feelings of guilt, extends throughout the whole family unit. Increased interest has, not surprisingly, resulted in a variety of imaginative theories and investigations aimed at offering at the very least a rational explanation to the bereaved parents, if not an avoidance of similar events. Little or no attention, however, has been paid to the precarious limitations of airflow present in children during the period of greatest risk of SIDS. All mammalian neonates drink milk and have an intranarial epiglottis. The larynx is both the narrowest and possibly the most vulnerable part of the upper airway in all species. Studies based on the histologic structure of over 100 infant larynges have shown that not only is the supraglottis largely composed of glandular tissue in all species, but glandular tissue is also found

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From the Institute of Laryngology and Otology, London, England.

Presented at the meeting of the American Laryngological Association, Palm Beach, Florida, April 28-29, 1990.

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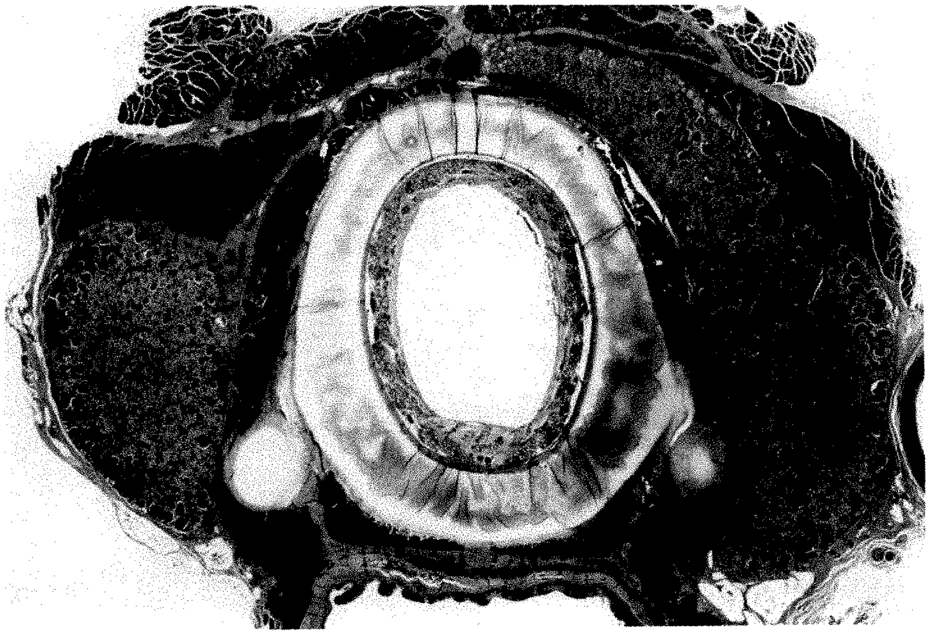

Fig 1. Transverse section through subglottis of boy who died of congenital heart disease at 3 months of age.

in the subglottis and upper trachea (Fig 1). In humans 3 months of age this tissue can represent a reduction in area from glottis to subglottis of 9.3 mm^2 to 7.0 mm^2, increasing to 8.5 mm^2 for the upper trachea.[3] Any increase in thickness of the subglottic subepithelial glandular tissue, when combined with increased viscosity of secretions, might seriously impair airflow. Humans are the only primates that leave their young unattended, and this fact may explain the apparent absence of SIDS in any other species, despite similar restrictions within the laryngeal complex. For example, in the sooty mangaby (*Cerecoebus torquatus*), the glottis averages 3.9 mm^2, the subglottis 2.8 mm^2, and the upper trachea 6.7 mm^2.

INVESTIGATION

In 1980, Fink and Beckwith[4] carried out estimations of the area of supraglottic mucous glands in infant larynges, expressing their results as a percentage of the total cross-sectional area of the supraglottic folds. Measurements were carried out on sectioned larynges from 13 infants who died of SIDS and 10 matched controls of comparable age who had died of noninfective conditions. There was a statistically significant excess of mucous glands in all SIDS larynges, which they felt might have been responsible for a fatal laryngeal spasm. My own comparative studies of mammalian infant larynges have confirmed the presence of a considerable amount of supraglottic mucous gland tissue that assists in providing protective bulk to the aryepiglottic folds.[5] However, the supraglottic area is far greater than the subglottis in this age group. A similar increase in glandular tissue, together with a possible increase in mucous viscosity within the subglottis, could therefore lead to lethal reduction in airflow. After some lengthy negotiations, supplies of SIDS larynges and tracheas were obtained from a number of pediatric pathologists throughout the United Kingdom. Full details accompanied each specimen, which had been fixed in 10% formaldehyde. Serial transverse sections at 6 μm were cut at supraglottic, glottic, subglottic, and first tracheal ring levels. Staining was with hematoxylin and eosin for area measurement utilizing a Measuremouse Image Intensifying system (Analytical Measuring System, Cambridge, England). This allows accurate reproducible measurement of a wide variety of parameters viewed on a visual display unit via microscopic camera. The total subglottic subepithelial area was measured and expressed as a percentage of the maximum subglottic area; in addition, figures for the actual subglottic area were calculated by the program.

A wide variety of specific staining techniques are also being employed to determine the constitution of the mucous secretions by means of aldehyde fuchsin–alcian blue, high diamise–alcian blue, and aluminum sulfate–alcian blue. Results from these studies are not yet available but hopefully will assist in determining whether there is increased viscosity in some or all of the larynges.

RESULTS

Although 74 SIDS larynges were available for sectioning and measurement, the more uncommon "control" specimens, removed from children of comparable age but dying primarily of congenital cardiac disease, only totalled 19. None proved of use in this investigation, since they had all been intubated for several days prior to death and subglottic mucosal damage was present in every specimen.

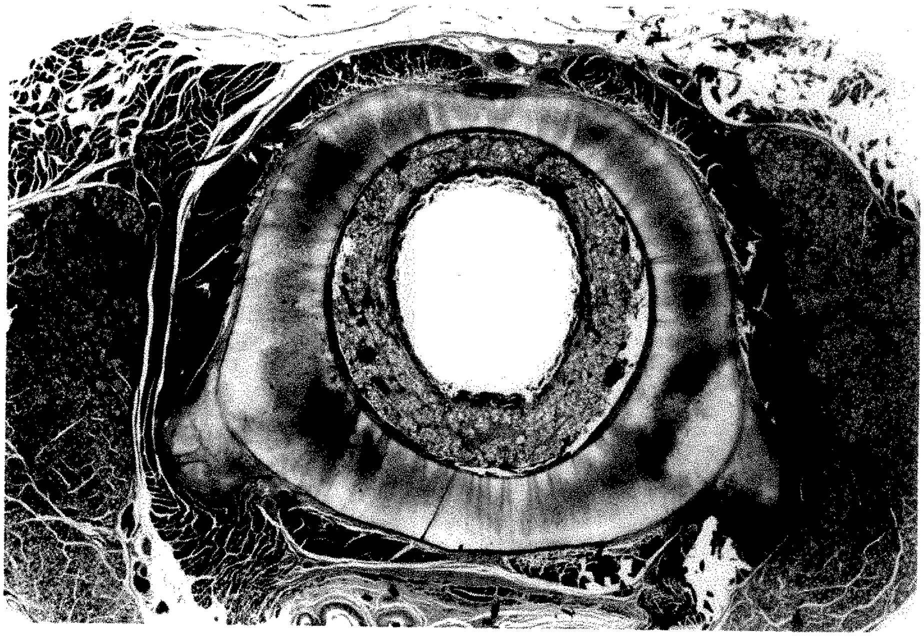

Fig 2. Transverse section through subglottis of boy who died of sudden infant death syndrome at 4 months of age. Note reduction of lumen by subepithelial glandular tissue.

In the event, the absence of "control" measurements proved less of a disadvantage than might be expected, since it was not envisaged that every SIDS larynx would show a significant increase in subglottic mucosal glands, nor was it possible to calculate what reduction in subglottic airway could be considered as hazardous — even lethal, perhaps! There was a male preponderance of 3:1 and the ages ranged from 2 weeks to 1 year, with the majority falling around 3 to 4 months. Weight at death ranged from a low of 1,710 g in a 14-week-old boy to a maximum of almost 10,000 g in the 1-year-old. Regression analysis showed no significant relationship between postmortem weight and maximum subglottic area nor, as might be expected, with the ratio between subglottic mucous gland and total subglottic area. However, within the group this ratio averaged at over 50%, varying from a low of 40% to a high of 87%. In the subject with the 87% ratio, a 20-week-old boy weighing 3,900 g, his residual subglottic airway was only 23 mm^2 — reduced from a theoretic maximum of 26 mm^2 (Fig 2).

DISCUSSION

There are, of course, many other factors to be considered, among which is a need for a large representative collection of "control" larynges in which the relationship between age and subglottic area can be evaluated. The term SIDS is manifestly unsatisfactory, both as a diagnosis, which it is not, and as an explanation to bereaved parents. This particular study does suggest that within this group of young children, some certainly have a significant reduction in their subglottic airway from an increase in mucus-secreting glandular tissue — possibly from a coexisting upper respiratory tract infection. If subsequent studies confirm that this secretion is of increased viscosity, then there must be a real possibility that some SIDS children die of anoxia. However, there is at present no significant measurement that can be made around the risk period that could identify high-risk children. Perhaps a late explanation to the parents of a cause of death may in itself be of value.

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PARTIAL LARYNGECTOMY AFTER IRRADIATION FAILURE

RICHARD D. NICHOLS, MD SAMUEL A. MICKELSON, MD

DETROIT, MICHIGAN

Forty-three patients who had partial laryngectomies after radiotherapy were evaluated. Forty-two had failed irradiation for laryngeal carcinoma. Nine had supraglottic procedures, 3 endoscopic, and 31 vertical partial. Twelve (28%) required subsequent completion laryngectomy. Major complications included laryngeal stenosis in 1, incompetent laryngeal sphincters in 2, mucocutaneous fistulas in 3, and delayed deglutition in 3. Six patients had positive permanent section margins. In 5 of those, intraoperative frozen sections had been taken and were negative. Recurrent or persistent disease was eventually demonstrated in all patients with positive margins. The 2-year determinant disease-free survival rate for stage I and II disease was 85%. Three-year disease-free survival was 50% for stage III and IV disease. Partial laryngectomies, including supraglottic, can be done after irradiation failure with a high expectation of cure and acceptable morbidity. Immediate additional operation should be considered in patients with positive margins.

KEY WORDS — laryngectomy, partial laryngectomy, radiotherapy, recurrent tumor, squamous cell carcinoma.

Limited carcinoma of the larynx can be treated with irradiation or partial laryngectomy. Certain patients fail primary treatment with either modality. Our standard protocol is that patients eligible for vertical partial laryngectomy are treated with irradiation primarily, with partial laryngectomy reserved for failures. The exception is that supraglottic laryngectomy is often recommended instead of irradiation for primary treatment of supraglottic tumors. We reviewed our experience with partial laryngectomy salvage of 18 irradiated patients in 1980[1] and concluded that such a protocol produced an excellent cure rate. There was some concern about incision of irradiated cartilage, but the study revealed acceptable postoperative morbidity as well.

We have treated 25 additional patients with partial removal of the larynx after irradiation and report our experience with all 43 patients in this communication.

MATERIALS AND METHODS

Forty-three consecutive patients who had partial laryngectomies after irradiation of the larynx during the years 1961 to 1988 were evaluated. Forty-two of the patients had failed irradiation given as primary treatment for carcinoma of the larynx and contiguous areas. One patient was treated with 60 Gy after radical removal of the right submandibular gland for adenocarcinoma. The larynx was in the treatment field for the duration of the irradiation. That patient is included in the evaluation of morbidity of partial laryngectomy after irradiation but not in the estimate of tumor control possible with partial removal of the larynx after irradiation failure.

There were 40 men and 3 women ranging in age from 44 to 75 years. The dose of radiation ranged from 60 to 70 Gy. Stage of the disease at diagnosis was 33 stage I, 6 stage II, 1 stage III, and 3 stage IV. None of the patients with stage III and IV disease had impaired vocal cord mobility. One had T2N1M0 disease (stage III). Three had T4 primary tumors (stage IV), in each case because of extension of disease outside the larynx.

The tumors originated in the glottis in 33 patients, the supraglottic pyriform sinus in 1, and the supraglottic larynx or immediately contiguous area in 9.

The interval between conclusion of irradiation and recurrence or persistence of tumor ranged from 1 to 191 months with a mean of 22.8 months and a median of 10 months. Twenty-seven or 65% of the patients had recurrences within 12 months, 32 or 76% had recurrences within 24 months, and 3 patients or 7% were considered to be free of disease for more than 60 months after irradiation.

The surgical procedures performed are listed in Table 1. Fourteen patients had cordectomies. The majority of those patients did not have removal of laryngeal cartilage. Nine had supraglottic laryngectomies. Six of those were considered to be extended operations, usually with removal of portions of the base of the tongue. In one patient, the involved side of the base of the tongue was excised to the region of

TABLE 1. SURGICAL PROCEDURES

Cordectomy		14
Frontolateral laryngectomy		11
Supraglottic laryngectomy		9
Extended operation	6	
Anterovertical laryngectomy		4
Laterovertical laryngectomy		2
Epiglottectomy		1
Endoscopic removal of tumor		2
Total		43

From the Department of Otolaryngology, Henry Ford Hospital, Detroit, Michigan.

Presented at the meeting of the American Laryngological Association, San Francisco, California, April 1-2, 1989.

REPRINTS — Richard D. Nichols, MD, Dept of Otolaryngology, Henry Ford Hospital, 2799 W Grand Blvd, Detroit, MI 48202.

TABLE 2. STATUS OF PATIENTS WHO HAD STAGES I AND II

Living with no evidence of disease		29
>5 y	22	
2 to 5 y	4	
<2 y	3	
Died with no evidence of disease		4
Living with disease		1
Indeterminate status		1
Died with local disease		3
Total		38

the foramen cecum. Eleven patients had frontolateral laryngectomies, four had bilateral anterovertical partial laryngectomies, and two had classic hemilaryngectomies. A portion of the anterior aspect of the laryngeal cartilage was removed with the soft tissue in all patients who had anterovertical operations. In the majority of frontolateral and hemilaryngectomy patients, the internal perichondrium of the thyroid ala was removed, leaving the cartilage itself in place. All but one of the patients in the last three groups had laryngoplasties using bipedicle flaps of strap muscle to replace the excised intralaryngeal soft tissue.

One patient had a transoral epiglottectomy and two had endoscopic removals of their limited tumors.

Evaluation of the status of surgical margins in the resected specimens was undertaken to ascertain the value of that information in regard to prediction of recurrence of disease.

RESULTS

No patients were lost to follow-up. Five of the 43 patients have died with disease. In 2 of these, the tumor origin was glottic. It was supraglottic in 3. Stage at the time of diagnosis in these 5 patients was stage I in 1 patient, stage II in 2, and stage IV in 2. The interval from partial laryngectomy to death was less than 12 months in 1, more than 24 months in 2, and more than 36 months in 2. Three of the 5 required completion laryngotomies. In two of the deaths associated with supraglottic tumors there was recurrence of disease in the larynx and the neck. In one, only the neck was involved.

One patient is living with known persistent disease. He is more than 2 years post-supraglottic laryngectomy and neck dissection with disease only in the neck. Another patient, nearly 2 years post-frontolateral partial laryngectomy, is considered to have an indeterminate status. He is a diabetic with a right sixth nerve palsy that has been extensively investigated and is of unknown cause.

The status of the 38 patients with stage I and II recurrent carcinoma is summarized in Table 2. Twenty-nine patients are living without evidence of disease, or lived more than 5 years without disease. Twenty-six of these are more than 2 years post-partial laryngectomy, 24 more than 3 years, and 22 more than 5 years. Four patients died without laryngeal disease, 3 patients died with local disease, and 1 patient is living with disease. The status of 1 patient is considered indeterminate nearly 2 years post-partial laryngectomy, with the patient having undergone a completion laryngectomy. For purposes of computation of survivorship, he is considered to have persistent disease. The 2-year determinant disease-free survivor rate, therefore, is 85%. The absolute disease-free 2-year survival rate is 80%.

All four patients with stage III and IV disease had supraglottic tumors and supraglottic partial laryngectomies. Two of the four patients are 3 years or more after partial laryngectomy and disease-free. One of the four required a completion laryngectomy. That patient eventually died with disease, as did another with recurrence only in the neck. The 3-year disease-free survival rate for patients with stage III and IV disease, therefore, is 50%.

Biopsy Cures. In 5 of the 42 patients treated surgically for recurrent disease, the partial laryngectomy specimens showed no evidence of disease. Tissue that had been taken for biopsy prior to the partial laryngectomies was reexamined and the presence of invasive tumor confirmed in each instance. The original stage of disease in these 5 patients with "biopsy cures" was stage I in 3 and stages III and IV in 1 each. The operations included two cordectomies, one frontolateral laryngectomy, one anterovertical laryngectomy, and one supraglottic laryngectomy with left radical neck dissection. This last patient's positive biopsy was obtained 2 years after radiotherapy and the operation had excised all sites of his original disease.

Completion Laryngectomy. Subsequent total (completion) laryngectomy was required in 12 patients (28%) because of recurrence of disease after partial laryngectomy. The origin of disease in these 12 patients was glottic in 11 and supraglottic in 1. Ten had stage I disease at the time of original diagnosis, 1 stage II, and 1 stage IV. The interval from irradiation to recurrence in this group ranged from 2 to 14 months with a mean of 7 months. The interval between partial laryngectomy and total laryngectomy was 1 to 49 months with a mean of 11 months. Three of these 12 patients eventually died with regional disease. Survivors without disease include 4 more than 5 years post-partial laryngectomy and 1 in each of these categories: more than 4 years, more than 3 years, more than 2 years, and less than 1 year. The status of 1 of the 12 patients is considered indeterminate nearly 2 years post-partial laryngectomy because of an unexplained sixth nerve palsy.

Surgical Margins. In 37 of the 43 patients, information was available on surgical margins of the partial laryngectomy specimens. In 6 of the 37 individuals, permanent sections showed positive mar-

TABLE 3. COMPLICATIONS

Perichondritis (stenosis)	1
Laryngocutaneous fistula	2
Pharyngocutaneous fistula	1
Incompetent sphincter	2
Delayed deglutition	3

gins. Five of the 6 had had intraoperative frozen sections. They were all negative. One of these patients had a total laryngectomy within 1 month of the partial operation because of the extent of margin involvement. The completion specimen showed residual tumor in both sides of the larynx. The patient was followed up for more than 5 years and was living without disease at that time. One patient was considered to have carcinoma in situ at the surgical margin of the frontolateral specimen. He underwent direct laryngoscopy and biopsy of the laryngeal area after healing had occurred. No tumor was found. Laryngectomy was required for recurrent tumor 51 months later. He is living without disease 57 months post–partial laryngectomy.

In the four remaining patients with positive permanent margins, no immediate additional treatment or diagnostic procedures were instituted. One patient, with a supraglottic primary extending into the base of the tongue and who had had an extended supraglottic laryngectomy and right radical neck dissection, experienced recurrence in the resected side of the neck 34 months after that operation. He refused additional treatment and died with local disease 40 months after his partial laryngectomy. Another patient required completion laryngectomy 6 months following partial laryngectomy and is living without disease 31 months post–partial laryngectomy. The fifth patient, with negative frozen and positive permanent margins, required completion laryngectomy for recurrence 7 months after the partial operation, and is living more than 1 year after the partial laryngectomy. In the individual who did not have frozen sections done, recurrence was seen in the neck 28 months after supraglottic laryngectomy. He had a left radical neck dissection in which 3 of 17 nodes were positive. Tumor emboli were seen in small veins and large lymphatics. He is currently undergoing chemotherapy for persistent disease.

No information was available about margins in 3 of the 12 patients who required subsequent total laryngectomy. Margins were positive in 4 of the 12 patients, with 1 of these considered to have carcinoma in situ. Margins were negative for carcinoma in the remaining 5 patients.

Surgical margins were negative in four of the five patients who have died with local disease. This group includes three who had subsequent completion laryngectomies.

Complications. Significant complications (Table 3) included one case of postoperative perichondritis and subsequent stenosis of the larynx, three mucocutaneous fistulas that required surgical closure, two larynges that were incompetent sphincters, and three cases of delayed deglutition. Remote flaps were required for closure of two of the fistulas. The third was closed with a local flap. One of the patients with an incompetent sphincter had had a hemilaryngectomy with excision of the laryngeal cartilage. Teflon injection of the larynx did not improve his status. We recommended completion laryngectomy, which he refused. He had a gastrostomy and died without evidence of laryngeal disease more than 4 years after his partial laryngectomy. The other patient with an incompetent sphincter had an extended supraglottic laryngectomy for a high pyriform sinus lesion. A pectoralis myocutaneous flap was required for closure. The left vocal cord was immobile following operation. The patient with perichondritis and subsequent laryngeal stenosis had had an extended supraglottic laryngectomy with excision of one of the arytenoids and continued to smoke and drink heavily following her operation. She required a tracheostomy but was able to eat and talk until her death from cirrhosis more than 5 years after the partial laryngectomy. All but two of the major complications occurred in patients who had supraglottic laryngectomies.

DISCUSSION

Historically, total laryngectomy was considered to be the only surgical option in the irradiated larynx because of concern for the complications associated with partial resection of irradiated cartilage and difficulty in assessing limits of persistent or recurrent disease. Papers in what might be considered contemporary literature continue to report total laryngectomy used essentially exclusively in the treatment of laryngeal carcinoma recurrent after irradiation.[2-5] Those who considered only patients who had irradiation for stage T1 and T2 disease reported salvage rates of 59% and 68%.[2,3] The concept of doing partial laryngectomy in patients eligible for such operations on the basis of extent of persistent or recurrent disease after irradiation failure, however, is not new. Som[6] reported 4 such patients in 1951. Our earlier publication[1] reported our experience with 18 patients and reviewed that of Som and six other authors.[7-12] The greatest experience reported was by Biller et al[9] (20 patients). Most reported 6 or fewer patients. Biller et al might be considered to have initiated contemporary consideration of this subject because of their enumeration and discussion of indications and contraindications for such operations. All authors reported excellent success rates with properly selected patients.

Advocacy of partially resecting the irradiated larynx for recurrent disease continued through the 1980s in several papers.[13-18] Sixty-five patients were reported by Sorenson et al.[14] Fifty-five of these had vertical and 10 had horizontal partial laryngectomies. They reported an 81% survival rate in patients who had vertical operations. Burns et al[15] reported a determinant survival rate of 70% and a completion laryngectomy rate of 25%.

Our early experience with partial laryngectomy salvage of patients who had undergone irradiation for limited laryngeal carcinoma indicated that it was a satisfactory approach to the treatment of laryngeal carcinoma in patients eligible for partial laryngectomy. Disease control rates were high and morbidity was acceptable. We became more aggressive in considering patients for such treatment but had some concerns about identifying the logical limits of such a protocol on the basis of what we considered less than optimal treatment outcomes in occasional individual patients. Analysis of this larger patient group, however, seems to justify the confidence engendered by the earlier review.

Of most concern is the experience with the evaluation of margins in partial laryngectomy. These are small specimens that should be oriented for the pathologist in their fresh state in order to obtain the most accurate evaluation. None of the patients in this study left the operating room with positive frozen margins. Subsequent demonstration of persistent or recurrent disease in all six who had positive margins on permanent sections justifies an immediate completion laryngectomy in future patients with that finding.

The patients who had supraglottic laryngectomies form a special subgroup, since some authors have expressed concern about whether or not postirradiation supraglottic laryngectomy patients can be rehabilitated. Sorenson et al,[14] for example, reported that they were able to restore only 2 of 10 patients to full functional status following horizontal laryngectomy after radiotherapy. Six of the nine operations that we reported here were extended, excising portions of the base of tongue, pharynx, or, in one case, an arytenoid. Two patients had mucocutaneous fistulas and others experienced delayed deglutition, but only 1 had aspiration with eating severe enough to prevent meaningful oral intake. That patient had had removal of part of the pharynx and a remote flap for reconstruction, and one side of the larynx was immobile after the operation. Another patient who had had a supraglottic laryngectomy extended to removal of an arytenoid had a stenotic larynx related to postoperative perichondritis. The larynx was not an adequate respiratory organ but was functionally sound as a sphincter and for speech. Seven of the patients had entirely functional larynges. Two had partial function.

There is some support in this review for a measured approach to postirradiation supraglottic resection, since this group comprises 21% of the 42 patients and is responsible for 60% of the deaths, the only patient known to be living with disease, and all but two of the major complications. The preponderance of mortality and morbidity can be explained in part by the fact that all patients with stage III and IV disease are in the supraglottic group.

CONCLUSIONS

Partial laryngectomies can be done in patients eligible for the operations who have failed radiotherapy for carcinoma. These procedures, including supraglottic laryngectomies, can be done with a high expectation of control of disease and with limited morbidity. Partial laryngectomy should be considered the operation of choice for patients eligible for it on the basis of anatomic extent of recurrent or persistent disease. If surgical margins are positive, immediate additional operation should be done. Completion laryngectomy will be required for subsequent recurrence in approximately one quarter of patients. This protocol will produce a disease control rate at least as high as that that would be achieved if total laryngectomy were considered the only option for such recurrence.

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CHOLESTEROL CYSTS OF THE TEMPORAL BONE: DIAGNOSIS AND TREATMENT

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Cholesterol cyst (or granuloma) of the temporal bone, a recognized clinical entity distinct from cholesteatoma, is more common than previously thought. Apparently it is caused by obstruction of previously pneumatized temporal bone air cells. Surgical cure is achieved by drainage and reestablishment of normal pneumatization. This paper reviews 14 cholesterol cysts of the temporal bone, emphasizing the importance of preoperative imaging and surgical approach. Use of magnetic resonance imaging differentiates cholesterol cysts from cholesteatoma or other neoplasms. Computed tomography delineates the location of the lesion and defines temporal bone anatomy essential to surgical approach. The two studies together allow the surgeon to properly plan drainage, as in the case of a cholesterol cyst, versus excision or exteriorization, as in the case of cholesteatoma. The infralabyrinthine approach to a petrous apex cholesterol cyst is the procedure of choice when hearing preservation is desired.

KEY WORDS — cholesterol cyst, granuloma, temporal bone.

INTRODUCTION

Cholesterol cyst (or granuloma) of the temporal bone is a recognized clinical entity distinct from cholesteatoma and more common than previously thought.[1] The pathophysiology appears to be initiated by obstruction of previously pneumatized temporal bone air cells. Surgical cure is achieved by drainage and reestablishment of normal pneumatization.[2] This paper is a retrospective analysis of 14 patients with a cholesterol cyst of the temporal bone. The importance of preoperative imaging and surgical approach will be emphasized. Magnetic resonance imaging (MRI) allows for accurate diagnosis, differentiating cholesterol cysts from cholesteatoma or other neoplasms. Computed tomography (CT) delineates the extent of the lesion and defines temporal bone anatomy essential to the surgical approach. The two studies together allow the surgeon to properly plan drainage, as in the case of a cholesterol cyst, versus excision or exteriorization, as in the case of cholesteatoma.

PATIENTS AND METHODS

A retrospective review of 18 consecutive patients with a diagnosis of cholesterol cyst of the temporal bone was performed at the New York University Medical Center in New York. Fourteen of these 18 patients had a surgically proven cholesterol cyst and constitute the data base for this review. All patients were treated by the two senior surgeons (R. A. Hoffman and N. L. Cohen) over the 14-year period 1975 to 1989.

The patient data accumulated included age at the time of operation, sex, initial symptoms, location of lesion, preoperative and postoperative radiographic evaluation, surgical approach, recurrence, and complications.

RESULTS

A summary of the clinical presentation, radiographic evaluation, and surgical management of 14 patients with a pathologically confirmed cholesterol cyst of the temporal bone is shown in Table 1. The age at the time of diagnosis ranged from 12 to 77 years, with a mean age of 36.8. There was a female preponderance, with a female to male ratio of 11:3. Two of the 9 patients with a petrous apex cholesterol cyst had a history of otologic disease and/or surgical procedures on the ipsilateral side, while 2 of the 5 with middle ear cholesterol cysts had a significant otologic history.

The presenting symptoms of these 14 patients are summarized in Table 2. The most common chief complaint was hearing loss; other frequent presenting symptoms were tinnitus and imbalance. Audiometric evaluation consistently showed a conductive hearing loss in those patients with a middle ear cholesterol cyst. However, those patients with petrous apex involvement exhibited normal, mixed, or sensorineural hearing loss patterns upon audiometric examination.

Computed tomographic examination of cholesterol cysts within the middle ear demonstrated an amorphous soft tissue mass without evidence of ossicular or petrous bone erosion. The CT examinations of cholesterol cysts of the petrous apex demonstrated smooth erosion of the contours of the apex by a mass that appeared isodense to brain parenchyma. Neither the middle ear nor petrous apex cholesterol cysts enhanced with intravenous contrast. The

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TABLE 1. REVIEW OF PATIENTS WITH CHOLESTEROL CYSTS OF TEMPORAL BONE

Case	*Age*	*Sex*	*Initial Symptoms*	*Location of Lesion*	*Preoperative Radiographic Evaluation*	*Year of Diagnosis*	*Surgical Approach*	*Radiographic Follow-up*
1	39	F	Hearing loss, aural pressure	Petrous apex	CT, MRI	1986	Infralabyrinthine	MRI
2	37	M	Tinnitus, headache, imbalance	Petrous apex	CT, MRI	1989	Infralabyrinthine	MRI
3	35	F	Hearing loss	Petrous apex	CT, MRI	1989	Infralabyrinthine	MRI
4	17	F	Otalgia	Middle ear, mastoid	CT, MRI	1988	Tympanomastoidectomy, M & T	PE
5	38	F	Tinnitus, headache, vertigo	Petrous apex	CT, MRI	1988	Infralabyrinthine	MRI
6	43	F	Facial paresthesia, tinnitus, headache	Petrous apex	CT, MRI	1988	Infralabyrinthine	MRI
7	32	F	Hearing loss, tinnitus, vertigo, facial paresthesia	Petrous apex	CT, MRI	1988	Suboccipital	MRI
8	77	F	Hearing loss, vertigo, headache	Petrous apex	CT, MRI	1986	Translabyrinthine	MRI
9	67	M	Hearing loss	Middle ear, mastoid	CT, MRI	1988	Tympanomastoidectomy	PE
10	43	M	Hearing loss, facial paresthesia	Petrous apex	CT, MRI	1983	Infralabyrinthine	CT, MRI
11	17	F	Tinnitus	Middle ear	CT	1988	Tympanotomy, M & T	PE
12	64	F	Hearing loss, tinnitus, vertigo	Middle ear	Tomogram	1975	Tympanotomy, M & T	PE
13	12	F	Asymptomatic	Middle ear	CT	1980	Tympanotomy, M & T	PE
14	32	F	Hearing loss, aural pressure, imbalance, tinnitus	Petrous apex	CT, angiogram	1979	Infralabyrinthine	CT

Only case 6 had recurrence, treated by translabyrinthine approach, and complications (profound hearing loss and facial paralysis).

CT — computed tomography, MRI — magnetic resonance imaging, M & T — myringotomy and tube placement, PE — physical examination.

MRI examinations of all cholesterol cysts demonstrated a well-circumscribed mass with high signal intensity (hyperintense to brain) on both T1- and T2-weighted images.

Five patients with a cholesterol cyst of the middle ear were treated via tympanotomy with myringotomy and tube placement, with or without mastoidectomy. The nine patients with a cholesterol cyst of the petrous apex were treated via three approaches: infralabyrinthine (seven), translabyrinthine (one), and suboccipital (one).

Postoperative follow-up ranged from 1 to 10 years and was usually achieved with serial MRI scans. One patient suffered complete loss of hearing on the operated side after infralabyrinthine marsupialization of a petrous apex cholesterol cyst. This patient also developed a delayed progressive facial nerve paralysis and recurrence of disease 2 months postoperatively. The patient was ultimately cured of disease by means of the translabyrinthine approach. This case represents the only recurrence and the only surgical complication in this series. Two representative cases are presented below.

CASE REPORTS

CASE 2

A 37-year-old man complained of a 3-month history of right-sided tinnitus with intermittent imbalance and headaches. He had no previous otologic history. Findings on physical examination of the head and neck and cranial nerves were normal.

An audiogram revealed normal hearing with a 100% speech discrimination score bilaterally. An MRI scan was then performed and it demonstrated a lesion of the right petrous apex with increased signal intensity on both T1- and T2-weighted images (Fig 1). A CT scan revealed a nonenhancing 2.5-cm lesion of the right petrous apex with evidence of bony remodeling of the clivus and erosion of the porus acusticus. The lesion appeared isodense with brain parenchyma. In addition, the jugular bulb was abutting the cyst, but not dehiscent, the mastoid cavity was well aerated and developed, and the intratemporal carotid artery was in a normal position (Fig 1). The preoperative diagnosis was that of a cholesterol cyst of the right petrous apex.

The patient underwent a right transmastoid infralabyrinthine approach to the petrous apex with drainage of the cholesterol cyst. It was noted intraoperatively that the cyst was in close proximity to the anterior and medial wall of the jugular bulb. Hence, to gain access to the cyst for adequate drainage, the jugular bulb was compressed inferiorly. A Silastic stent was placed into the cyst and brought out into the mastoid for permanent aeration. Postoperatively the patient did well, with no change from his preoperative audiogram. A follow-up MRI scan 12 months after the operation showed a de-

TABLE 2. PRESENTING CLINICAL SYMPTOMS (N = 14)

Symptom	*No. of Patients*
Hearing loss	9
Tinnitus	7
Vertigo or imbalance	6
Facial paresthesia	3
Otalgia or aural pressure	3
Hemorrhagic otorrhea	1

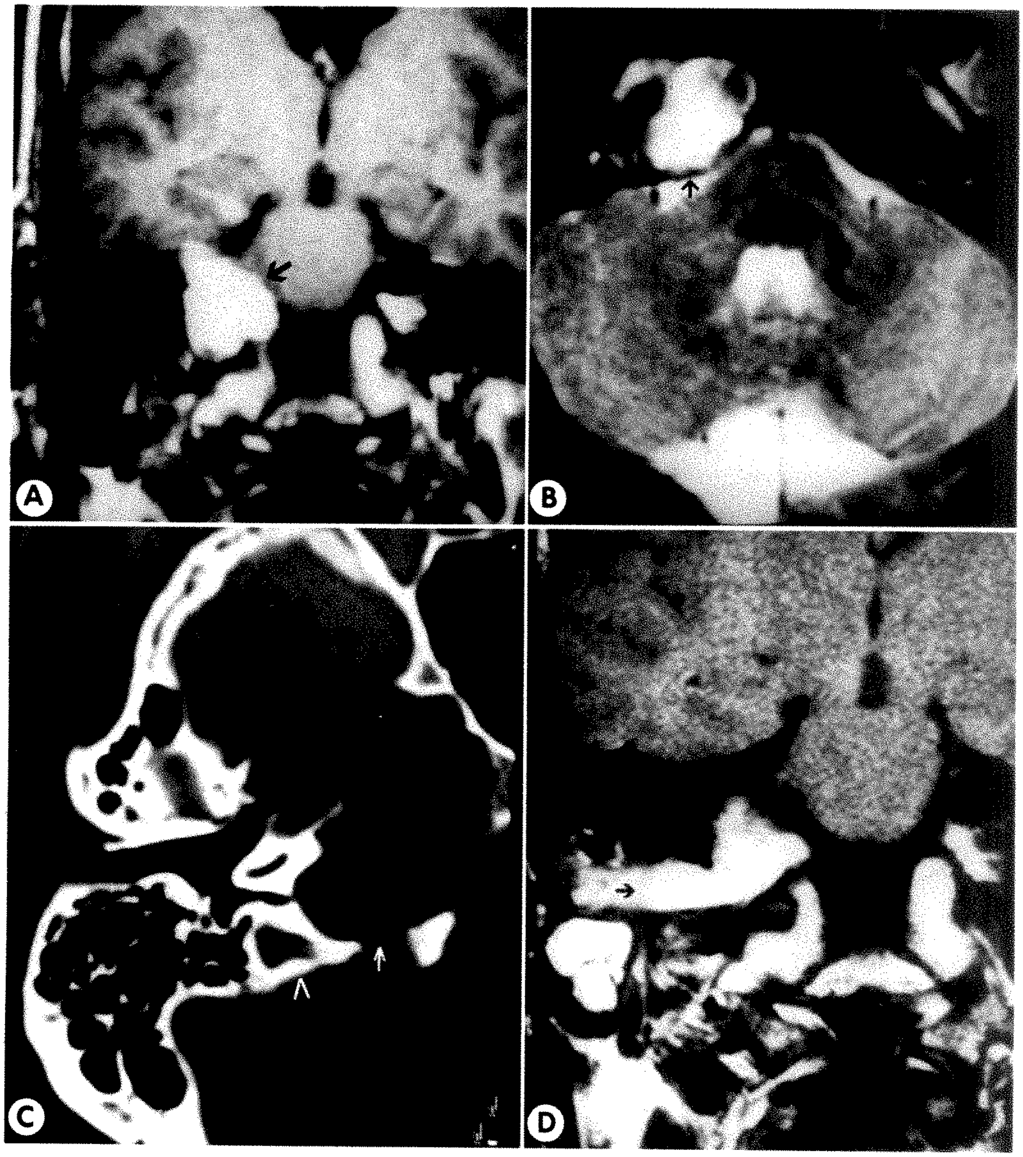

Fig 1. (Case 2) A) Preoperative T1-weighted magnetic resonance image showing high-intensity right petrous apex lesion (arrow). B) Preoperative T2-weighted magnetic resonance image showing high-intensity right petrous apex mass (arrow). C) Preoperative computed tomogram with contrast revealing nonenhancing right petrous apex lesion with remodeling of clivus and destruction of porus acusticus (arrow). Note position of jugular bulb (arrowhead). D) One-year-postoperative T1-weighted magnetic resonance image revealing decrease in size of mass. Note high signal intensity (arrow) within Silastic sheeting consistent with continued functional drainage of cyst.

crease in size of the previously noted cholesterol cyst with decreased signal intensity on T1-weighted images. These findings confirmed that the lesion was successfully evacuated (Fig 1).

Comment. This case represents a typical presentation of a petrous apex cholesterol cyst. The preoperative workup included an audiogram, a CT scan, and MRI. Findings on the radiographic evaluation were consistent with a cholesterol cyst. Therefore, an infralabyrinthine approach was selected to treat this patient because he had normal hearing and excellent speech discrimination.

CASE 4

A 17-year-old girl complained of a 9-month history of right-sided otalgia, bloody otorrhea, and hearing loss. Relevant otologic history included chronic ear infections and allergies. Upon physical examination a dark blue bulging tympanic membrane with dried blood in the attic was noted. The remainder of the findings on physical examination, including cranial nerve function, were normal.

An audiogram revealed a right-sided mild conductive hearing loss with pulsations on the tympanogram. A CT scan demonstrated near-total opacification of the tympanic cavity by a soft tissue mass. The ossicular chain appeared intact. The mastoid air cells were also opacified by abnormal soft tissue. No areas of bone destruction were identified. The intratemporal carotid artery and jugular

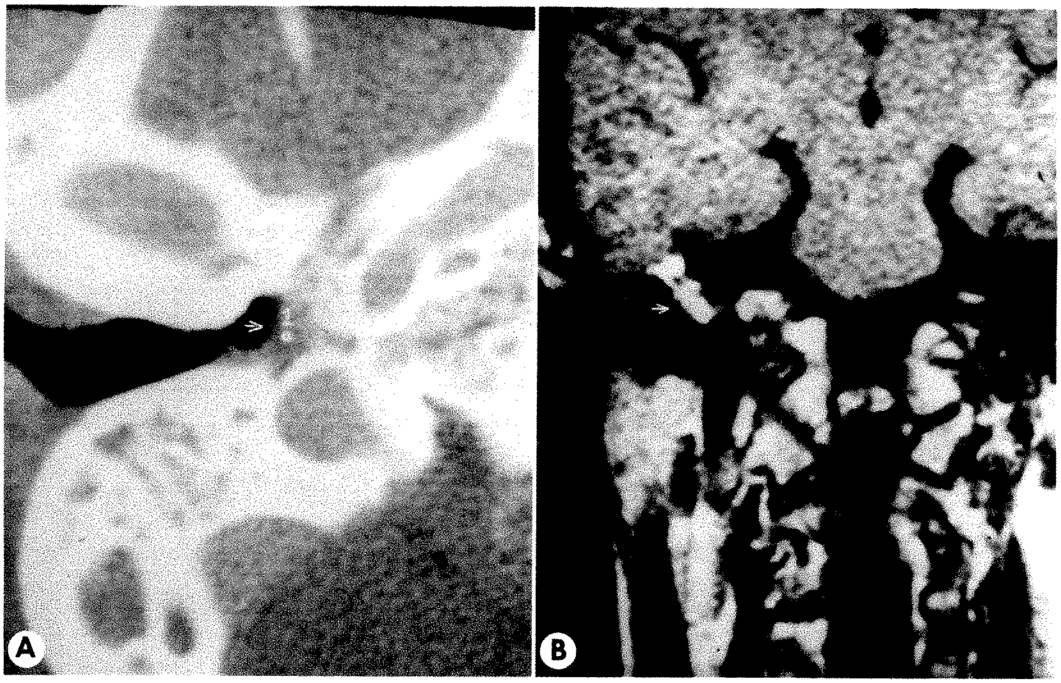

Fig 2. (Case 4) A) Preoperative computed tomogram with contrast demonstrating nonenhancing middle ear mass (arrow). B) Preoperative T1-weighted magnetic resonance image demonstrating high-intensity middle ear mass (arrow).

vein were in a normal position (Fig 2). A T1-weighted MRI scan demonstrated that a small area of the mastoid and the entire tympanic cavity contained a mass of high signal intensity. That no signal void was noted within the middle ear mass excluded a glomus tympanicum tumor (Fig 2). These findings, coupled with those of the physical examination, suggested a chronic inflammatory process of the mastoid and middle ear with a combination of cholesterol cyst and granulation tissue.

The patient underwent a right tympanomastoidectomy with placement of a ventilation tube. Granulation tissue and brown oily fluid were found in the middle ear space and mastoid cavity. One year later, the patient is without recurrence of her disease.

Comment. The differential diagnosis of a blue, bleeding mass in the middle ear includes a glomus tumor, a high-riding jugular bulb, and an aberrant internal carotid artery. Solitary cholesterol cysts have also been reported to mimic vascular lesions of the middle ear.[3] This case emphasized the importance of preoperative radiographic evaluation when treating such lesions. The CT scan revealed a soft tissue density without evidence of bone destruction within the middle ear cleft, excluding a dehiscent jugular bulb or an aberrant carotid artery.

Magnetic resonance imaging characterized the nature of the soft tissue within the tympanic cavity, differentiating cholesterol cyst from granulation tissue and possible glomus tympanicum. A signal void on T1-weighted MRI would suggest blood flow.[4] Therefore, a lack of signal void would rule out a vascular tumor. Thus, a tympanomastoidectomy with placement of a ventilation tube was performed without complication.

DISCUSSION

Cholesterol cyst, also known as cholesterol granuloma, forms as a result of a foreign body giant cell reaction to cholesterol crystals.[5] It was first described by Manasse[6] in 1894. Proposed factors in the pathophysiology of cholesterol cysts include hemorrhage, interference with drainage, and inadequate aeration. The lesions are commonly encountered in the middle ear and mastoid air cells after obstruction of the normally aerated spaces due to associated diseases such as otitis media or cholesteatoma. The term idiopathic hemotympanum is used to clinically describe the precursor of a cholesterol cyst of the middle ear.[7] Previous otologic procedures or local trauma may also be predisposing factors.[8] Cholesterol cysts of the petrous apex are not necessarily associated with other ear disorders. They grow slowly over a period of years and do not come to clinical attention until they reach a critical size and impinge upon surrounding structures.[9] The natural degradation of blood yields by-products that include cholesterol crystals. These crystals initiate a foreign body reaction that results in granuloma or cyst formation.[5] The cyst wall is made up of fibrous connective tissue and lacks the keratizing squamous epithelium seen in cholesteatoma. The cholesterol cyst contains brown-yellow fluid with oily, globular material, lipids, and cholesterol crystals. The color comes

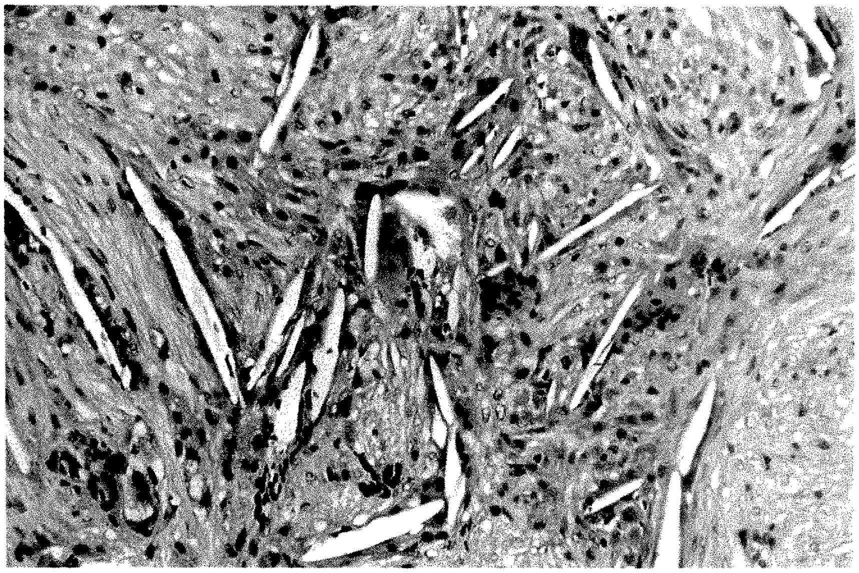

Fig 3. Cholesterol cyst characterized by foreign body giant cells, chronic inflammatory cells, and fibrosis (H & E, original x250). Empty spaces result from dissolution of lipid cholesterol by alcohols of tissue preparation process.

from hemosiderin deposits. When viewed microscopically the cyst contents reveal cholesterol crystals surrounded by foreign body giant cells[5] (Fig 3).

The signs and symptoms of a cholesterol cyst of the temporal bone are related to anatomic location. Thus, cholesterol cysts of the middle ear tend to be small and are detected early owing to their associated symptoms such as hearing loss and ease of physical examination. Lesions at the petrous apex typically present with cranial nerve compression. Cerebellopontine angle syndrome with involvement of cranial nerves V through VIII and cerebellar findings are common in petrous apex lesions.[5]

The differential diagnosis depends upon the location of the lesion. A "blue" lesion of the middle ear must be differentiated from a dehiscence of the jugular bulb, an aberrant carotid artery, or a glomus tumor.[10] Lesions of the petrous apex include cholesteatoma, meningioma, schwannoma, glomus tumor, cartilaginous tumor, lymphoma, histiocytosis X, and arachnoid cyst. Other space-occupying lesions include carotid aneurysms and mucoceles. Developmental anomalies and metastatic disease may also occur in this area.[11] The surgical approach and extent of surgical extirpation are dictated by tumor type, size, and extension. The cholesterol cyst is best managed by marsupialization and establishment of normal pneumatization, not total removal.

Audiometric evaluation is helpful but nonspecific. The hearing test will determine the extent of hearing loss and may reveal useful information as to the site of the lesion. Six of our nine patients with petrous apex cysts showed a sensorineural hearing loss. Preoperative imaging is the key to the diagnostic evaluation. Computed tomography characteristically demonstrates a sharply marginated expansile lesion with remodeling and erosion of bone. These lesions are avascular, do not enhance with contrast, and are isodense with brain tissue. These characteristics exclude all lesions of the petrous apex other than cholesteatoma and mucoceles.[11] Computed tomographic scanning is also essential in delineating the extent of the lesion and planning the best surgical approach. Important preoperative considerations include the status of the intratemporal carotid artery and jugular bulb, and the limits that a particular patient's temporal bone anatomy might impose on the surgical approach.

Magnetic resonance imaging has provided a valuable adjunct in preoperative differential diagnosis of a petrous apex mass. Cholesterol cysts are unique in that they demonstrate high signal intensity on both the T1- and T2-weighted images that is presumably due to cholesterol crystals and chronic hemorrhagic by-products.[4] This finding differs from that of MRI evaluation of cholesteatoma of the petrous apex, which demonstrates medium signal intensity on T1-weighted images and high signal intensity on T2-weighted images. Thus, the evaluation of these cysts by CT scan and MRI are complementary; in combination they provide important information regarding diagnosis and planning of the surgical procedure and preoperative diagnosis[12] (Table 3). Since the cysts are bright on both T1- and T2-weighted images, gadolinium-ethylenediaminetet-

TABLE 3. IMAGING MODALITIES

	Cholesterol Cyst	*Cholesteatoma*
Computed tomography		
Margins	Sharp, smooth	Sharp, smooth
Density	Isodense to brain	Isodense to cerebrospinal fluid
Enhancement	No	No
Magnetic resonance imaging		
T1-weighted signal intensity	High	Low
T2-weighted signal intensity	High	High

raacetic acid is not necessary.

Careful follow-up of these patients is essential. We have found MRI scanning the image modality of choice for follow-up in that it delineates soft tissue structures at the petrous apex. The decreased signal intensity on T1-weighted images reflects the successful evacuation of cholesterol crystals and hemorrhagic products from the cyst.[4] Thus, the preoperative MRI can be compared to the postoperative scans to follow the course of the affected region. Middle ear cases can be followed by otoscopy.

The goal of treatment for cholesterol cysts of the temporal bone is drainage and permanent aeration. Total removal is not necessary for definitive treatment owing to its lack of epithelial lining. Permanent fistulization can be accomplished through either the mastoid or the middle ear, if the eustachian tube is patent. If the eustachian tube is dysfunctional, aeration can be maintained through a ventilation tube or an exteriorized mastoid cavity.[5]

The surgical approach to the petrous apex cholesterol cyst depends upon the location of the lesion and the status of the patient's hearing. If no usable hearing is present a transcochlear[13] or translabyrinthine[14] approach can be employed. If hearing is to be preserved, a suboccipital, middle cranial fossa, infratemporal fossa, transsphenoid, or infralabyrinthine approach may be used.[15] Although the suboccipital approach was used in one patient in this series, in whom the cyst was isolated to the area of the internal auditory canal, it does not provide permanent drainage or aeration. This isolated cyst could be totally excised. In addition, contamination of the subarachnoid space by the contents of the cholesterol cyst might incite a chemical meningitis. Therefore, this approach is not generally recommended, except for such unusual presentations. The middle cranial fossa approach is an extradural approach to the petrous apex. Drainage of the cyst can be achieved, but permanent aeration is not possible; therefore, recurrence is likely.[15] Fisch[16] has described the infratemporal fossa approach to the apex of the petrous bone. The cyst is drained, the petrous apex is obliterated, and the external auditory canal is closed laterally as a blind sac. This procedure is technically difficult and results in a conductive hearing loss. If the lesion abuts the posterior wall of the sphenoid sinus the transsphenoid approach may be used.[12] Limited exposure, proximity of the internal carotid artery, and difficulty in maintaining a fistula for aeration are disadvantages of this procedure.[15]

We have found that when hearing is to be preserved, the transmastoid infralabyrinthine approach is the procedure of choice. This procedure provides a direct path for aeration of the petrous apex through the mastoid inferior to the labyrinth, posteromedial to the facial nerve, and inferior to the internal auditory canal. The cyst is identified, incised, drained, irrigated, and stented open into the mastoid cavity with rolled Silastic sheeting. If this pathway becomes obstructed and the cyst recurs, the surgical defect may be easily reexplored and reestablishment of aeration attained.

When an infralabyrinthine approach is planned, CT is an essential adjunct to MRI. While MRI allows for the preoperative diagnosis of a cholesterol cyst, only CT demonstrates the regional anatomy necessary for safe exploration. In particular, it is important to know the location of the jugular bulb, the facial nerve, and the internal carotid artery. In addition, one must also realize the degree of mastoid pneumatization and localization of the sigmoid sinus. Knowledge of these anatomic landmarks ensures relatively safe infralabyrinthine exploration.

CONCLUSION

Cholesterol cysts require careful preoperative evaluation including CT and MRI scanning and audiometry. The surgical approach must be tailored to the extent of the lesion and the status of hearing. The various surgical approaches are discussed to achieve the goal of drainage and permanent aeration. The middle ear and mastoid can be treated with tympanotomy and ventilation tube with or without mastoidectomy. For petrous apex cysts, with hearing preservation as a preoperative therapeutic goal we feel the infralabyrinthine approach is the procedure of choice. The MRI scan provides accurate preoperative diagnostic evaluation and the CT scan provides important anatomic information. In fact, MRI is probably responsible for the apparent increased incidence of this entity. It is the radiographic modality of choice for follow-up.

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PATTERNS OF PHYSICAL AND SEXUAL ABUSE OF COMMUNICATIVELY HANDICAPPED CHILDREN

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Evidence suggests that handicapped children are at increased risk for abuse and neglect. Communicatively impaired youngsters are particularly vulnerable because of their limited ability to report the maltreatment. Of 482 abused handicapped children evaluated at Boys Town National Research Hospital, 212 had hearing impairment, 87 speech language disorders, 39 learning disorders, 43 behavioral-emotional disturbances, 74 mental retardation, 5 visual impairment, 3 cleft lip or palate, and 19 other disorders. The perpetrator was either a relative or a "trusted other" in 97.2% of sexual abuse cases. Handicapped males were much more likely to be victims of sexual abuse than nonhandicapped males in the general population. Children being educated in residential schools were more likely to be sexually abused than mainstreamed youngsters. These children may be at risk for abuse from a wide variety of potential perpetrators, including teachers, dormitory counselors, van drivers, clergy, classroom aides, older students, peer siblings, scout leaders, abused peers, baby-sitters, and custodians.

KEY WORDS — child abuse, communicative disorders.

INTRODUCTION

Depending upon the definitions of maltreatment used in the report, incidence figures for child abuse and neglect in the general US population in 1986 ranged from 16.3 to 25.2 per 1,000, which converts into 1 to 1.5 million child victims.[1] Cases of abuse and neglect increased by 66% over the 1980 figures, reflecting an increase of 74% in the incidence of abuse. Part of this increase may be attributable to more accurate reporting by health care providers and agencies. The most frequently reported category of maltreatment was physical abuse, followed in order by emotional abuse and sexual abuse.

Although the issue of child maltreatment has risen to a high level of public awareness during the past decade, surprisingly little attention has been afforded children with handicaps.[2] The handicapped population is the largest minority group in the United States. In 1986, the US Census Bureau estimated 37 million handicapped individuals age 15 and older, compared to 29 million blacks and 17 million Hispanics. During the 1987-1988 school year, 4.4 million children with disabilities were provided special education assistance in the United States.[3]

Abuse of handicapped children is a reprehensible occurrence that attracts media attention when it is reported. Many states have had major child abuse investigations in residential schools and institutions for the hearing impaired, visually impaired, and mentally retarded.[4] Professionals, including child protection workers, believe handicapped children to be at high risk for abuse and that some disabling conditions are caused or exacerbated by maltreatment.[5,6] However, there is a surprising paucity of methodologically sound research in both the general and handicapped abuse fields.[2] Existing literature addressing the problem can be categorized under three major headings: the perception of high incidence rates by service providers, the proportion of children with handicaps within a sample of abuse victims, and the proportion of abuse victims within a sample of handicapped children.

Perception of High Incidence Rates by Service Providers. Handicapped children are presumed to increase stress among parents and thereby increase their risk of being maltreated.[7,8] They may also be at special risk because of the very nature of their handicap.[8-13] Mentally retarded children may be at greater risk given that ordinary standards of care are inadequate for them.[14] Many handicapped children exhibit behavioral characteristics such as tantrums, aggressiveness, and noncompliance that impact negatively on parents and caregivers, increasing their risk for abuse.[15]

Signs and symptoms of abuse are difficult to recognize in certain handicapped children. The communication problems inherent in many disabilities may render children unable to understand or verbalize episodes of abuse.[16,17] Many handicapped children and their families display characteristics asso-

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ciated with abuse in nonhandicapped populations, including poverty, poor coping abilities, and a parental history of abuse.[18,19] The major weakness of this body of research is that it represents anecdotal reports and perceptions and, accordingly, may not reflect the true magnitude of the problem.

The hypothesis that the child's handicap plays some process role in maltreatment has yet to be addressed empirically. It may be that certain handicaps are greater risk factors than others and that interactions between specific handicaps and caretaking roles exist. Finkelhor et al[20] found that the majority of day-care abuse occurs around toileting. Sullivan et al[21] found that in deaf youth, sexual abuse tended to occur in bathrooms, beds, and specialized transportation. Current educational practices may also play contributory roles in maltreatment, ie, inadequate sex education, condoned physical interventions that can escalate to abuse, and insistence on compliance.

Proportion of Children With Handicaps Within a Sample of Abuse Victims. Among studies that have reported a high incidence of handicapped children in maltreated populations are those of Gil[22] (22%), Birrell and Birrell[23] (26%), Lightcap et al[24] (43%), Mian et al[25] (66%), and Johnson and Morse[26] (70%). Among incest victims, high incidences of abnormal electroencephalograms and handicapping conditions have also been reported.[27,28] The limitations of this research are that broad and nonspecific criteria were used in identifying handicapping conditions, as well as abuse, and that data in the records reviewed were anecdotal since handicaps were identified by subjective impressions of record reviewers. Disparities in criteria for handicapping conditions and abuse may explain why some research has failed to find disproportionate percentages of handicaps in abused samples.[29] One study found no differences between abused and nonabused children in terms of congenital defects or birth injuries,[30] and a study completed by the Iowa Department of Social Services[31] found a 4% incidence rate of mental retardation and physical impairment among abused children.

Proportion of Abuse Victims Within a Sample of Handicapped Children. High incidence rates of sexual abuse among the mentally retarded, ranging from 25% to 83%, have been reported. Other handicapping conditions have been investigated, and sexual abuse rates have included 20% of cerebral palsied youngsters,[32] as well as 23% and 50% among two populations of hearing-impaired children.[21] Perceptions of high rates of physical and sexual abuse have been reported for blind,[33,34] chronically ill,[35] schizophrenic,[36] and multihandicapped (R. T. Ammerman et al, unpublished observations, 1987) children. Various handicapping conditions, including mental retardation,[37] cerebral palsy,[38] developmental delays,[39] speech and language handicaps,[40] and multiple personality disorder[41] have been attributed to abuse and neglect. Unfortunately, these studies did not have large enough pools of data to preclude subject selection biases. Institutional impediments to the identification and reporting of abuse in residential institutions, including schools for the deaf, may be partially accountable for underreporting of cases.[4]

Nearly half of the states in the United States do not collect any information on special characteristics, including handicaps, of abused and neglected children, and the remaining half exhibit variability in style and competence of collection techniques.[42] Although a majority of child protective service workers believe handicapped children are at increased risk for maltreatment, most have never served handicapped clients.[5] In a West Virginia sample of identified child abuse victims, 70% were found to have handicapping conditions and 35% had handicaps attributed to the maltreatment.[43] Nebraska is one of the few states that codes handicapping conditions of children referred to child protective services and in out-of-home placements.

The available data base on abuse among handicapped populations is flawed by differing operational definitions of maltreatment, disparate methodologic strategies, heterogeneous handicapped populations, and questionable validation procedures for handicapping conditions.[2,29] The present report is based on data gathered as part of a longitudinal study of therapeutic efficacy among a group of abused children with documented and verified handicapping conditions. It augments previous reports[16,21] of preliminary data from the Center for Abused Handicapped Children at Boys Town National Research Hospital.

METHODS

The study population consisted of 482 (274 male, 208 female) consecutively referred children and adolescents with identifiable handicapping conditions and documented maltreatment who were evaluated at the Center for Abused Handicapped Children at Boys Town National Research Hospital over a 4-year period. Subjects ranged in age from infancy to 21 years (mean age = 7.5 years; mode = 12 years) at the time of the initial episode of maltreatment. Categorized by racial heritage, the group consisted of 8.4% blacks, 84% whites, and 7.6% others, including Native Americans. Patients were referred from 18 states and one Canadian province, with the majority coming from states in close proximity to Boys Town National Research Hospital's location in eastern Nebraska. Types of maltreatment included one or more of the following: sexual abuse, physical abuse, combined sexual and physical abuse, emotional abuse, and neglect. Study children were categorized by handicap as follows: hearing impairment (n = 212), speech and/or language

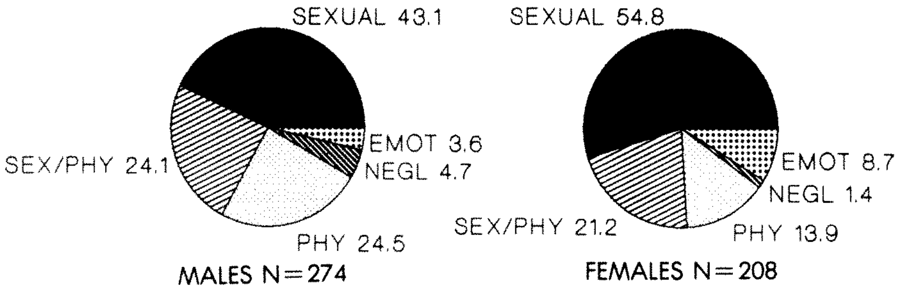

Fig 1. Percentages of types of abuse for abuse study population (N = 482). EMOT — emotional, NEGL — neglect, SEX — sexual, PHY — physical.

impairment (n = 87), learning disability (n = 39), mental handicap (n = 74), behavioral disorder (n = 43), and other disabilities, including cleft lip or palate, cerebral palsy, juvenile rheumatoid arthritis, etc (n = 27). As part of an ongoing longitudinal study of treatment efficacy, an extensive data base was developed that incorporated data regarding characteristics of victims and perpetrators, locale or site of abuse, severity of abuse, and temporal pattern of abuse episodes. Communicatively handicapped children from both mainstream and residential programs were evaluated and comparisons were made between variables for the two groups.

The demographic characteristics of the subjects and the perpetrators were investigated by means of descriptive statistics, including frequency counts and percentages, as well as means and standard deviations when appropriate. In addition to the computation of descriptive statistics, χ^2 tests of independence were conducted on each of the variables paired with the type of abuse variable.

To establish the reliability of recording coding procedures, 55 records were randomly selected and reviewed by a second hospital staff member. Intercoder agreement was computed by using Cohen's κ coefficients for a subset of the variables included in the study. The κ coefficients for the 10 variables included in the reliability analysis ranged from .70 to 1.00, with an average of .90, indicating strong agreement between the coders.

RESULTS

The most prevalent type of maltreatment reported for both gender groups of victims in the study population was sexual abuse: 43% of the males, 54.8% of the females, and 48% of the total group (Fig 1). In descending order of frequency, the categories of abuse experienced by the study children were as follows: sexual, sexual and physical, physical, emotional, and neglect. This finding contrasts sharply with data reported for nonhandicapped populations of youngsters, in which the most often reported type of maltreatment is physical abuse, followed in order by emotional and sexual abuse.

Although sexual abuse was the most common type of maltreatment experienced by communicatively handicapped females in the study, whether they were being educated in a mainstream (42.2%) or residential setting (72.2%), an important difference was observed among communicatively handicapped males. Mainstreamed boys were somewhat more likely to be physically abused (35%) than sexually abused (30%), but males in residential institutions were much more likely to be sexually abused (58.8%) or sexually and physically maltreated (28.9%) than to suffer isolated physical abuse (10.5%). The large number of male sexual abuse victims in the total study population, as well as within the male study population itself, is also at variance with data from the general population of infants to 21-year-olds, which reveal a preponderance of sexually abused females. In the general pop-

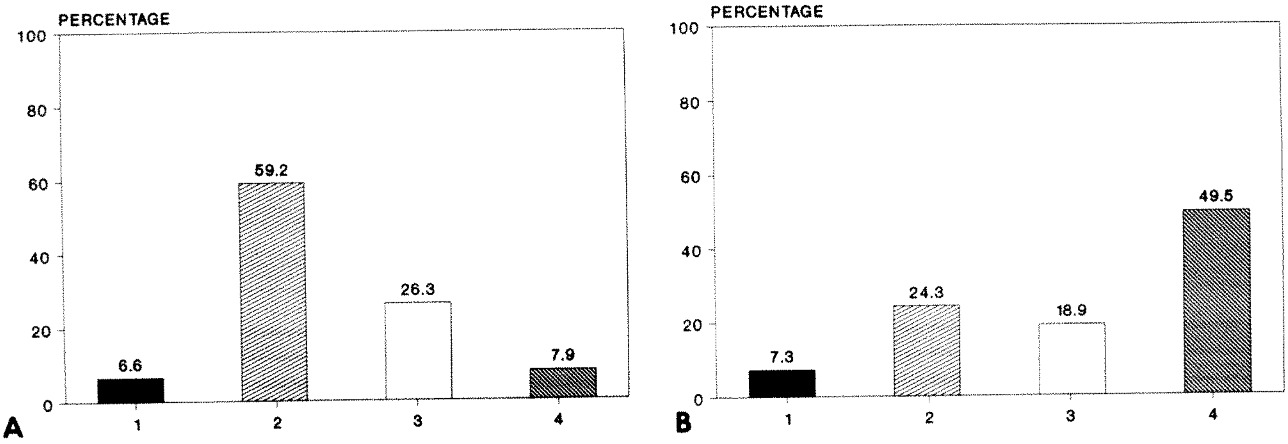

Fig 2. Severity of A) physical and B) sexual abuse. See text for definition of categories.

TABLE 1. FEMALE PERPETRATOR CHARACTERISTICS

	Type of Abuse			
Perpetrator	*Sexual*	*Physical*	*Emotional*	*Neglect*
Parent	21.0%	68.0%	71.4%	93.8%
Teacher	4.8%	10.3%	9.5%	0.0%
Houseparent	24.2%	7.2%	0.0%	0.0%
Older child	14.5%	0.0%	0.0%	0.0%
Sibling	14.5%	2.1%	0.0%	0.0%
Peer	11.3%	0.0%	14.3%	0.0%
Relative	6.5%	2.1%	4.8%	0.0%
Stepparent	0.0%	6.2%	0.0%	6.3%
Step-sibling	0.0%	0.0%	0.0%	0.0%
Stranger	0.0%	0.0%	0.0%	0.0%
Other	3.2%	4.1%	0.0%	0.0%

TABLE 2. MALE PERPETRATOR CHARACTERISTICS

	Type of Abuse			
Perpetrator	*Sexual*	*Physical*	*Emotional*	*Neglect*
Parent	14.2%	50.0%	50.0%	77.8%
Teacher	0.4%	4.0%	7.1%	0.0%
Houseparent	15.3%	13.8%	0.0%	0.0%
Older child	18.4%	0.6%	0.0%	0.0%
Sibling	5.4%	3.4%	0.0%	0.0%
Peer	18.6%	4.6%	35.7%	0.0%
Relative	6.1%	1.7%	3.6%	11.1%
Stepparent	3.1%	6.3%	0.0%	11.1%
Step-sibling	1.9%	0.0%	0.0%	0.0%
Stranger	2.1%	0.0%	0.0%	0.0%
Other	14.4%	15.5%	3.6%	0.0%

ulation, males are much more likely to be physically maltreated than sexually abused.

Sexual abuse was also the single most frequently reported type of maltreatment among each of the handicap-specific subgroups: hearing impaired (53.4%), speech impaired (55.0%), learning disabled (41.0%), behaviorally disordered (32.0%), mentally retarded (39.0%), and other (40.7%).

Severity of physical abuse was classified according to the following scheme (Fig 2A): 1) behavior potentially injurious to the child, 2) tissue-damaging event including harmful restraint or control, 3) serious injury requiring medical or dental services, and 4) fatality or life-threatening physical abuse. Among the children who suffered physical abuse, the type of maltreatment experienced fell within category 2 in 59.2% of cases. Category 3 maltreatment was reported in 26.3% of cases, category 4 in 7.9%, and category 1 in only 6.6% of subjects.

Severity of sexual abuse was also graded along a continuum (Fig 2B): 1) witnessing sexual abuse, 2) fondling, 3) oral, genital, or digital penetration or genital abuse without penetration, or 4) anal or vaginal intercourse or penetration. Of those children who suffered isolated sexual abuse, 49.5% experienced category 4 maltreatment, 24.3% category 2, 18.9% category 3, and 7.3% category 1. A similar pattern of sexual abuse was observed among the children who endured both sexual and physical maltreatment. Nearly 44% (43.8%) fell into category 4, 25.8% into category 2, 23.6% into category 3, and 6.7% into category 1.

Perpetrators were classified both by gender and by degree of relationship to the child (Tables 1 and 2). Sexual abuse was most often committed by male perpetrators (male = 88.5%; female = 11.5%), as was physical maltreatment (male = 64.1%; female = 35.9%). Males were somewhat more likely to be guilty of emotional abuse (male = 57.1%; female = 42.9%), but females were much more likely to be directly accountable for neglect (female = 67.5%; male = 32.5%). In examining perpetrator identity data for the present study population of abused handicapped children, it became evident that most of the perpetrators were familiar and "trusted" persons in the children's environment. The high percentage of familiar perpetrators was a consistent finding across the spectrum of maltreatment: sexual abuse (97.2%), physical abuse (100%), emotional abuse (98.0%), and neglect (100%). Strangers or "unknown" individuals accounted for no more than 3% of sexual abuse among this population of abused handicapped youngsters.

The type of abusive behavior most frequently attributable to female and male perpetrators was examined separately for each gender. When a female perpetrator was involved in sexual abuse, 42% were relatives of the children, subdivided as follows: parents (21%), siblings (14.5%), and other relatives (6.5%). Houseparents in residential schools or other institutions were responsible for 24.2% of sexual abuse perpetrated by females. With regard to male sexual abuse perpetrators, 25.6% were relatives of victims. Male residential houseparents (15.3%), older children (18.4%), and peers (18.6%) were all somewhat more likely to engage in sexual abuse than male biological or adoptive parents (14.2%). On the other hand, biological or adoptive parents accounted for 50% of physical maltreatment and emotional abuse and 77.8% of neglect perpetrated by males.

The temporal pattern of the abuse episodes suffered by each child was also analyzed. Only 17.4% of the sexually abused youngsters were victimized on a single occasion. The remaining 82.6% endured multiple episodes of sexual abuse over various time periods: 33.0% less than 1 year, 26.9% 1 to 3 years, and 22.7% greater than 3 years. Episodes of physical maltreatment tended to recur over somewhat longer time periods: 26.8% less than 1 year, 30.9% 1 to 3 years, and 34.9% greater than 3 years.

The site or locale at which various types of abuse occurred was studied (Fig 3). In considering all types of abuse collectively, the most frequent site at which maltreatment was perpetrated was the handicapped child's home (50.2%), followed in order by the school, including residential schools (28.7%), both home and school (7.3%), the perpetrator's home (6.3%), and other sites (8.1%). If one consid-

TABLE 3. SIGNIFICANT CHI-SQUARE TESTS OF INDEPENDENCE

Likelihood for Abuse	*df*	χ^2 *Value*	*p*
Males > females*	4	19.37	.0007
Attractive > unattractive*	4	15.97	.0031
Residential school > mainstream†	8	55.88	<.0001
Dormitory > other sites†	6	41.67	<.0001
Home > school or other sites§	20	79.70	<.0001

*Except for emotional abuse.

†For sexual abuse only.

§Except for sexual abuse.

ers the three most common types of abuse separately, an interesting pattern emerges. The child's home is by far the most common site at which isolated physical abuse was carried out (home = 73.3%; school = 14.4%). Combined physical and sexual abuse was also more likely to occur in the youngster's home (50.9%) than at school (25.5%), but the pattern reverses for cases of isolated sexual abuse, 39% of which happened at school (including residential school) and 34.7% occurred at home. The most common abuse site in residential facilities was the dormitory.

Statistical analysis revealed significant differences among some of the variables (Table 3). For all types of abuse, except emotional, a greater number of males were abused than females. In addition, for all types of abuse except emotional, abused children were considered to be physically attractive rather than unattractive by independent observers. Children who attended residential schools were significantly more likely to be victims of sexual abuse than children who attended school in mainstreamed settings. The location within the residential schools in which sexual abuse and sexual and physical abuse was most likely to occur was the dormitory at school. Likewise, sexually abused children were abused at both home and school, while children who suffered other types of abuse were more likely to be abused at home only.

CONCLUSIONS AND RECOMMENDATIONS

Unfortunately, sexual and/or physical abuse, together with emotional abuse and/or neglect, continue to be significant risks for children with communication disorders and related disabilities. The increased susceptibility of these youngsters (particularly males) to sexual abuse, compared to the general youth population, is most likely attributable to two factors: 1) education and child care practices and 2) communication barriers. Society's continuing practice of segregating many of these children into special schools and residential care facilities during their vulnerable, formative years removes many of the safeguards inherent in the supervision of a caring family.

The limited training and compensation provided to most caregivers in residential institutions for the deaf in the United States can impede implementation of the high-quality child care practices that have proven effective in state-of-the-art youth care facilities.[4] Pedophiles who are willing to trade financial reward for easy access to potential victims naturally gravitate toward child care positions in poorly financed and loosely structured institutions in which their criminal behavior is likely to escape detection. Deaf children with impaired communication skills who have been separated for educational reasons from the protection of their natural home environment undoubtedly provide a strong attraction for such perpetrators. Not only houseparents, but also other employees in schools, including van drivers, custodians, gardeners, etc, must be considered as possible perpetrators. Appropriate screening procedures should be implemented to minimize the chances that such individuals will be employed by facilities serving children. In addition, policies and procedures must be developed and enforced to guarantee the child's safety in educational, recreational, and residential environments.[4]

Many abuse prevention curricula developed for use with the general population of young children have focused on so-called "stranger danger." The children are cautioned against the threat posed by unfamiliar individuals as potential abusers and/or abductors. "Say no, go and tell" are the watch-

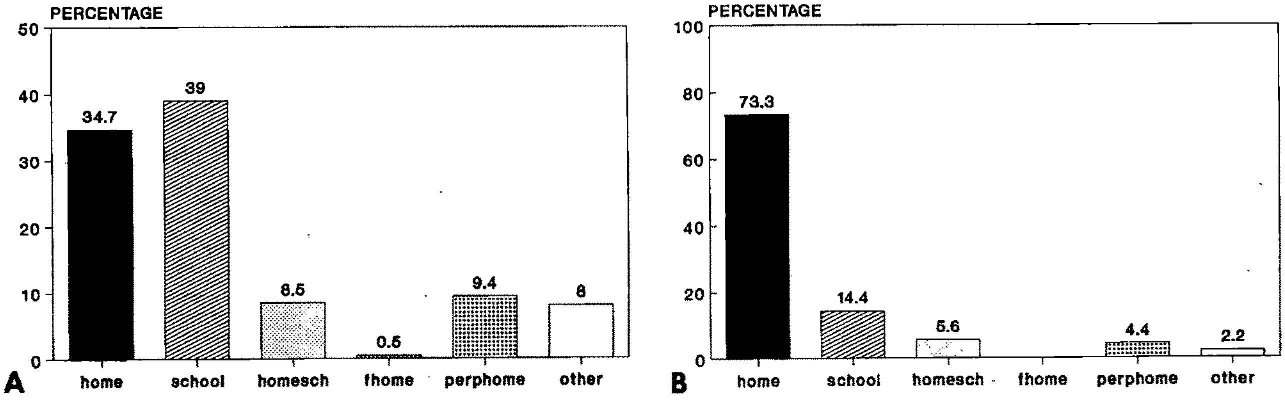

Fig 3. Sites of A) sexual and B) physical abuse. homesch — home and school, fhome — foster home, perphome — perpetrator's home.

words, even for programs aimed at deaf children, based on the assumption that the child will have ready access to a sympathetic, nonabusive parent or guardian. The very large number of "known and trusted" perpetrators involved in the sexual abuse of handicapped children reinforces the need for specially tailored abuse prevention strategies for this population.

In previous reports, the authors have stressed the important abuse-prevention role that must be played by members of the hearing health care team. Parents of hearing-impaired children must be helped to become psychologically prepared for the stress inherent in being the parent of a communicatively impaired child. Physical abuse can be reduced if parents find support from professionals and other parents and are counseled regarding acceptable alternatives for venting their anger and frustration, apart from physical maltreatment of their child. The demands of rearing a handicapped child are unrelenting, and special attention should be directed toward identifying neglect. Such behavior might be suspected from failure to keep scheduled appointments for needed medical or audiologic care, weight loss or failure to thrive in younger children, accompaniment of the child to outpatient visits by poorly informed or uninterested surrogate caregivers, or other evidence of lack of parental interest in the child's well-being.

It is the legal as well as ethical responsibility of all health care providers to report suspected child maltreatment to legal authorities, usually state child protective services. This responsibility becomes even more acute when the child has a communicative impairment and cannot self-report abuse episodes.

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COCHLEAR IMPLANTS AS A CONTRAINDICATION TO MAGNETIC RESONANCE IMAGING

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Magnetic resonance imaging poses little risk to the majority of patients undergoing scanning. However, cochlear implantation should pose a contraindication to this imaging process. This conclusion is based on several findings of in vitro testing of three cochlear implants: the 3M/House and 3M/Vienna designs and the Nucleus device. Specifically, tremendous torques are generated by each of these devices when they are introduced into the coil of a magnetic resonance imager; in addition, the 3M products not only were noted to induce an electrical current, but also were significantly magnetized and rendered afunctional. The clinical implications are discussed.

KEY WORDS — cochlear implant, magnetic resonance imaging.

INTRODUCTION

Magnetic resonance imaging (MRI) has revolutionized noninvasive diagnostic techniques by utilizing superconducting magnets and radio signals as opposed to ionizing radiation in order to generate images. Not only are the images produced of higher resolution and clarity than those produced by computed tomography, but the patient is spared exposure to potentially harmful doses of radiation. As such, MRI has become a widely used testing modality, posing little risk to the majority of patients undergoing scans. Of course, certain contraindications to its use do exist, and they are largely due to the tremendous magnetic fields inherent to this imaging process; these restrictions apply primarily to some pacemaker wearers and patients with particular cerebral aneurysm clips. Preliminary findings concerning MRI and cochlear implants were first reported by Mattucci et al[1] in an investigation of the effects of MRI on middle ear prostheses. The present investigation was undertaken to determine what the effects of MRI are on cochlear implants in vitro and assess whether or not this testing modality poses any hazards to patients who are cochlear implant recipients.

MATERIALS AND METHODS

Three different cochlear implants were included in the study. The first two were manufactured by 3M (3M Corp, Los Angeles, Calif), ie, the 3M/House and 3M/Vienna designs. The 3M/House design is a single-channel cochlear implant constructed with a rare earth (samarium cobalt) magnet at its center and 670 turns of 40-gauge copper wire surrounding it, with platinum-iridium (90-10) electrodes, insulated with silicone, and encapsulated in epoxy. The second, in contrast, is the 3M/Vienna design, a multichannel cochlear implant that has no ferromagnetic materials listed in its design, with seven turns of copper wire and 90-10 platinum-iridium electrodes, also encapsulated with epoxy and insulated with silicone. The third cochlear implant is the Nucleus device (Cochlear Corp, Englewood, Colo), again a multichannel implant, which consists of 22 platinum-iridium circumferential bands around a single tapered Silastic carrier. The Nucleus device has several ferromagnetic components used in its construction: a minimagnet used to align the transcutaneous external transmitter coil, a ferrite transformer, and an iron alloy lid used on the stimulator chip.

Each of the cochlear implants was then introduced into the coil of a 0.6-T superconducting magnetic resonance imager manufactured by Technicare (Solon, Ohio). The cochlear implants were suspended by a silk thread during T1- and T2-weighted imaging to determine deviation off the vertical, ie, deflection forces.

Next, the leads of the 3M cochlear implants were connected with several microfuses ranging from 2 to 100 mA in a series fashion, and again placed into the magnetic field of the imager. The Nucleus device, in contrast, had two terminals fashioned to its electrode by the manufacturer, which in turn were connected to a voltmeter well outside the imaging area. A Micronta voltmeter (Tandy Corp) was used; it has the capability of measuring a minimum of 0 to 300 mA (direct current). All the cochlear implants were returned to the manufacturers, along with the microfuses, and were examined to assess their function.

RESULTS

While in the magnetic field of the imager, all three cochlear implants showed a significant deviation off the vertical; specifically, the 3M/House device demonstrated a 60° deflection, the 3M/Vienna, a 10° deflection, and the Nucleus device a 53° de-

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flection. The actual rotational forces or "torques" generated by the enormous magnetic field varied considerably depending on the orthogonal orientation of the devices relative to the constant static magnetic field of the imager. On the basis of this observation, it was believed the value of the torque could not be quantitatively evaluated. Nonetheless, the torque was subjectively determined to be of significant magnitude that could easily dislodge the implant from its supporting foundation in vitro, and most certainly in vivo.

After careful examination by the manufacturer, both 3M devices were found to be significantly magnetized and "afunctional" as a result of their exposure to the magnetic resonance imager. In addition, all of the microfuses used were found to be overloaded or "burned out"; this finding indicates the induction of a minimum instantaneous current of at least 100 mA (direct current). The Nucleus device, in contrast, showed no current generated or change in magnetization or function.

DISCUSSION

Since the advent of MRI, few limitations or contraindications to its use have been established; hence, it is a diagnostic tool of enormous capacity. Naturally, much concern has been raised as to whether this imaging process poses any adverse biologic effects, since three powerful electromagnetic fields are generated during imaging.

1. A strong, static magnetic field, which remains virtually constant, is used to align the protons.
2. A small, rapidly varying magnetic field gradient is used for spatial localization.
3. Radio frequency pulses are used to produce changes in the energy states of the protons.

At present it is generally accepted that these magnetic fields pose no reproducible adverse effects upon living tissue if used within specified guidelines.[2] However, some contraindications to MRI exist in patients with ferromagnetic metallic implants or other ferromagnetic materials, largely because of the potential hazards associated with movement of these objects, as in the case of some aneurysm clips, which have been shown to become dislodged from clipped vessels in an animal model.[2] Other potential problems associated with MRI include heating of the material, the induction of electrical current, and the misinterpretation of artifact as an abnormality.[2] However, to date there have been no reports of induced electrical currents produced by MRI of metallic bioïmplants. Furthermore, the temperature changes associated with small metallic bioimplants and larger orthopedic prostheses were shown to be negligible.[3,4] In the case of cardiac pacemakers, the hazards seem to lie in the alteration of normal pulsing parameters that may be induced by the magnetic resonance imager.[5]

As outlined by Shellock and Crues[6] and Shellock,[7] several important factors influence the relative risk of using MRI in patients who have metallic biomedical implants. These include 1) the strength of the gradient and static magnetic fields, 2) the degree of ferromagnetism of the implant or material, 3) the geometry of the implant or material, 4) the location and orientation of the implant in situ, and 5) the amount of time the implant has been in place. In accordance with the laws of physics, magnetic materials align themselves in the direction of a static magnetic field, as evidenced by the aforementioned deflection forces. Clearly, when a magnetic material has changed its orientation within this static magnetic field, rotation forces will act to realign the material, generating significant torques, ie, rotational movements.

Since the cochlear implants have not previously been studied in conjunction with MRI, several findings from this investigation bear emphasis. They suggest that subjects with cochlear implants should not be exposed to the magnetic field of a magnetic resonance imager. First, significant electrical currents were generated by the 3M cochlear implants, which certainly could result in severe injury to the cochlea and its related structures. Next, significant forces were generated by all three of the cochlear implants that potentially could cause movement of the implant within the patient's head and, in doing so, injure surrounding structures, damage the electrode, or even withdraw the electrode from within the cochlea. Of course, the effect depends on the degree of fixation and the integrity of the surrounding tissues. Since the sensitivity of the cochlear implant relies on its ability to electrically stimulate specific regions of the cochlea, even the slightest change in position of the intracochlear electrodes could alter the specific signals generated, requiring, at least, reprogramming of the device.

The last consideration is the damage caused to the instrument itself, and not to the patient. After being exposed to what is now considered a relatively weak (0.6 T) magnetic resonance imager, both of the 3M cochlear implants were found to be significantly magnetized and afunctional; the Nucleus device, however, showed no loss of function and no change in magnetization. Other factors not brought out by our investigation but of consideration are the artifacts or "white-out" caused by the implant during imaging, which have been shown to be very significant, especially when magnetic materials are imaged,[2] and finally the potential for heat generation, which has not proved to be significant in other investigations.[3]

CONCLUSION

Previous studies have shown that most patients with metallic bioimplants (approximately 75%) can be examined relatively safely by MRI.[7] These bioimplants included aneurysm and hemostatic clips; dental implants and materials; intravascular coils, filters, and stents; middle ear prostheses[2,8,9]; prosthetic heart valves; orthopedic implants; penile implants; and other miscellaneous metallic implants and materials. The hazards of performing MRI on patients with metallic bioimplants usually related to movement or dislodgment, but potentially can relate to temperature change, induction of electrical current, and the misinterpretation of artifacts as an abnormality.

In the case of two 3M cochlear implants and the Nucleus device, we have shown the following primary effects:

1. Large torques are created that potentially can dislodge the cochlear implant and electrodes.
2. Significant electrical currents are generated in the 3M/House and 3M/Vienna cochlear implants when they are exposed to the magnetic field of a 0.6-T imager.
3. Exposure to the magnetic field renders the 3M devices magnetized and afunctional.
4. The Nucleus device maintains both function and magnetization after exposure to the magnetic field.

On the basis of these findings, MRI is contraindicated in patients with the cochlear implants reviewed. Further investigation is needed to determine if these findings can be applied to other models on the market today.

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SURGICAL MANAGEMENT OF TRACHEAL STENOSIS IN AN INFANT WITH MULTIPLE CONGENITAL ANOMALIES: WHEN IS BABY INOPERABLE?

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Congenital tracheal stenosis is a rare disorder that carries a significant morbidity and mortality. It is an even greater challenge when present in combination with other life-threatening congenital anomalies. We present an infant with multiple congenital anomalies, including trisomy 21, who was diagnosed with congenital tracheal stenosis at 3 months of age. At age 5 months, the infant underwent tracheoplasty with costal cartilage graft and pulmonary artery banding. Bronchoscopy 3 weeks later revealed a patent airway. However, the patient died 2 months postoperatively of cardiac complications. At autopsy, whole organ and histologic specimens revealed excellent incorporation of the graft with no evidence of re-stenosis. Our documentation of graft incorporation in this patient is evidence that long segments of stenotic trachea can be successfully treated by tracheoplasty utilizing rib cartilage grafts.

KEY WORDS — congenital tracheal stenosis, costal cartilage graft.

INTRODUCTION

Congenital tracheal stenosis was first described in the 19th century,[1] but did not receive much attention because of its rarity, its nearly uniform mortality, and the lack of successful treatment methods. In 1964, Cantrell and Guild[2] classified congenital tracheal stenosis into three categories: 1) generalized hypoplasia, 2) funnel-like stenosis, and 3) segmental stenosis. They described tracheal resection as treatment for the latter two categories and noted that "no satisfactory therapy appears available for the repair of the totally hypoplastic trachea." Majeski et al[3] in 1980 described costal cartilage graft tracheoplasty for tracheal stenosis in a pediatric burn patient, and Kimura et al[4] in 1982 described successful costal cartilage tracheoplasty in a 1-year-old with congenital stenosis of the entire trachea.

CASE REPORT

A full-term, 3,590-g boy was born to a 26-year-old woman (gravida 3, para 2); the delivery was by cesarean section because of fetal distress. Apgar scores were 1 and 7. Arterial blood gas analysis showed a pH of 7.35, a P_{O2} of 48 mm Hg, a P_{CO2} of 45 mm Hg, and an oxygen saturation of 81% on room air. He was immediately transferred to Yale–New Haven Hospital for further evaluation. An echocardiogram revealed an atrioventricular canal, type B, without evidence of an arterial band or sling. Chromosome analysis showed trisomy 21. His condition stabilized initially, but at 2 weeks of age he developed an increasing respiratory rate and feeding difficulty that was attributed to worsening congestive heart failure. Vomiting and aspiration were noted and corresponded to his cyanotic episodes. Gastroesophageal reflux was confirmed on pH probe studies. Severe cyanosis associated with reflux persisted despite medical treatment of reflux, and at the age of 3 months, a Nissen fundoplication and gastrostomy were performed. At this time it was found that a 3.5-mm endotracheal tube could not be passed beyond 1 to 2 cm below the vocal cords. Subsequent fiberoptic tracheoscopy confirmed tracheal stenosis, and fluoroscopy and plain tomograms showed that this stenosis extended to just above the carina. Rigid bronchoscopy revealed complete tracheal rings with a 1- to 2-mm tracheal lumen extending from 1 cm below the vocal cords to 1 to 1.5 cm above the carina. At the completion of the bronchoscopy the patient suffered a cardiac arrest and was successfully resuscitated.

He subsequently developed ischemic colitis, and worsening pulmonary and cardiac status required prolonged ventilation and numerous antiarrhythmic and inotropic agents. Over the ensuing weeks the child improved to the point at which discussion of further aggressive treatment was undertaken. At 5 months of age, the patient underwent pulmonary artery banding and tracheoplasty via a median sternotomy. The cardiac surgery team was prepared to perform cardiopulmonary bypass if needed, but this was not required. Ventilation during the procedure was maintained via an endotracheal tube that was advanced under direct vision to the level of the carina as the trachea was opened longitudinally. A segment of costal cartilage was harvested and split longitudinally. The two pieces were shaped to fit the defect in the trachea and were sutured in place

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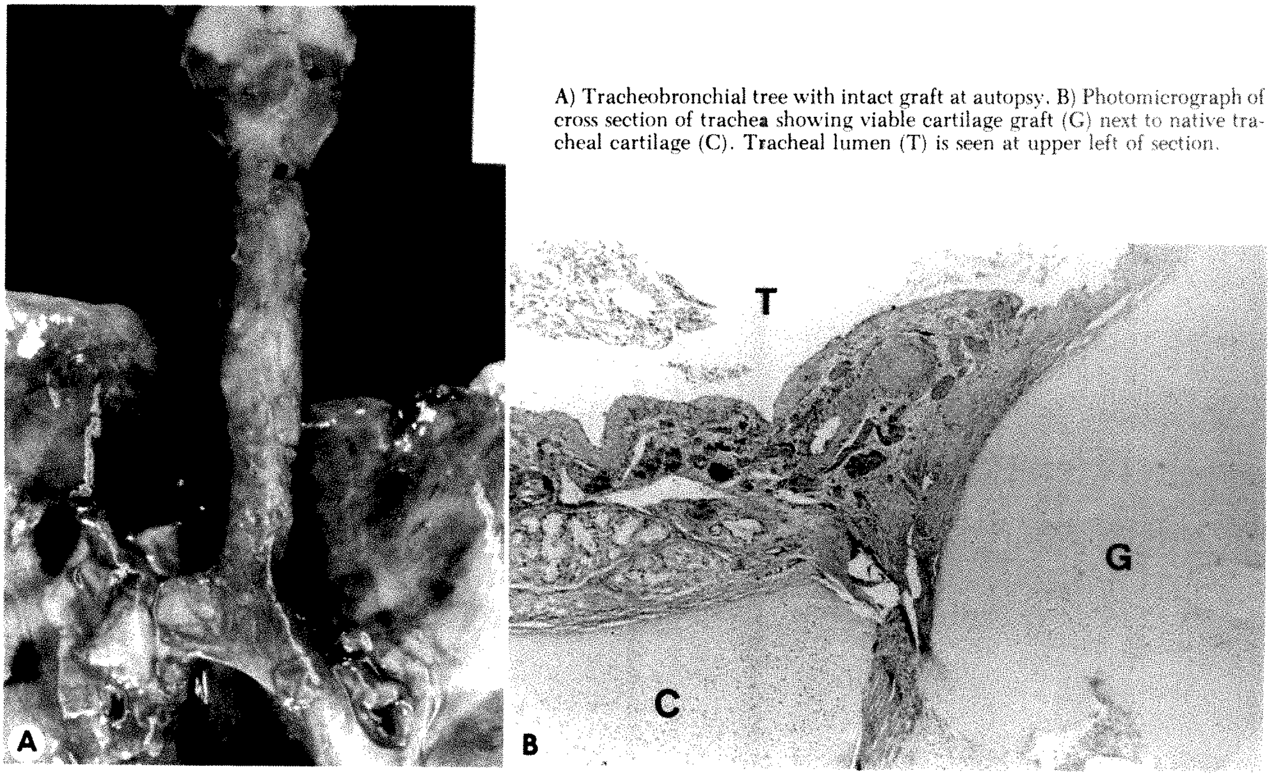

A) Tracheobronchial tree with intact graft at autopsy. B) Photomicrograph of cross section of trachea showing viable cartilage graft (G) next to native tracheal cartilage (C). Tracheal lumen (T) is seen at upper left of section.

with 4-0 Prolene sutures. The suture line was airtight with positive pressure, and the endotracheal tube was positioned past the repair with its tip distal to (above) the carina. The patient remained intubated and paralyzed postoperatively as planned for controlled ventilation, prevention of suture line disruption from neck movement, and use of the endotracheal tube as a stent.

Three weeks postoperatively bronchoscopy revealed a patent airway with an intact suture line. A 3.5-mm Storz-Hopkins bronchoscope passed to the carina easily. Bronchoscopy at 6 weeks showed complete healing of the suture line and no re-stenosis. Attempts to wean the infant from the ventilator were unsuccessful owing to ongoing cardiopulmonary disease, and he died on the 46th postoperative day. At autopsy, examination of the repaired trachea revealed excellent incorporation of the cartilage graft without evidence of re-stenosis (see Figure, A). Histologic examination also showed a viable cartilage graft with surrounding inflammatory changes at the suture line (see Figure, B).

DISCUSSION

Since the categorization of Cantrell and Guild[2] in 1964, considerable progress has been made in the surgical management of tracheal stenosis. The work of Grillo et al,[5,6] Maeda and Grillo,[7] and others[2-4,8-13] has shown that resection and primary anastomosis is the treatment of choice for strictures up to 50% of the length of the trachea. However, with stenosis involving more than about 50% of the tracheal length, mobilization of the trachea and larynx may not be enough to allow the ends to come together without excessive tension. Attempts at tracheal replacement have been disappointing. The most promising approach has been tracheoplasty involving longitudinal incision of the stenotic trachea and grafting to enlarge the tracheal lumen.[3,4,8,12,14,15] Many materials have been tried as grafts, including periosteum, esophageal wall, rib, dura, pericardium, and costal cartilage.[3,4,8,9,13-16] Each has its advantages and disadvantages, and experience with each has been limited. Permanent and absorbable prosthetic materials have also been tried, but infection, rejection, and extrusion have been major drawbacks. Costal cartilage appears to be well suited for this purpose given its local availability as an autologous living tissue, low metabolic requirements, ability to survive by diffusion of nutrients, semirigid nature and ability to be sculpted to the required size, and demonstrable incorporation into the tracheal tissues.[2-4,11,12] Although this infant eventually succumbed to his cardiac disease before the stenosis could be completely corrected, postmortem examination showed good incorporation of a viable graft without re-stenosis.

The incidence of other anomalies in children with congenital tracheal stenosis is quite high.[8,10,12,13] Our patient had multiple congenital anomalies, including trisomy 21, complete atrioventricular canal, and gastroesophageal reflux. These children should be thoroughly evaluated when possible for other life-threatening anomalies prior to any attempt at repair of the stenosis. In our patient it was difficult to determine which of his multiple problems was responsible for pulmonary hypertension and respiratory failure, or whether he had any chance of survival. After he had shown some improvement with intensive medical management, we decided that pulmonary banding and tracheoplasty should be performed before correction of the atrioventricular canal could have an acceptable chance of success. Only after multiple discussions with the medical specialists following him, as well as with the social workers and parents, was the decision made to operate.

Preoperative assessment of the trachea included fluoroscopy, simple tomograms, and direct rigid bronchoscopy. Several authors mention the need for a bronchogram to evaluate the intrathoracic trachea,[4,8,10-12] but placing contrast past a stenotic trachea in an infant can be dangerous. We found that careful fluoroscopy gave adequate definition of the proximal (lower) limit of the stenosis. We agree with Healy et al[17] that direct visualization of the trachea appears to give the best information.

SUMMARY

Congenital long-segment tracheal stenosis is rare. The presence of other anomalies that cause cardiopulmonary failure may make decisions about appropriate treatment even more difficult. Each patient must be considered individually. Anterior longitudinal tracheoplasty using costal cartilage grafts appears to be an effective treatment.

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DELAYED PHARYNGOESOPHAGEAL PERFORATION: A COMPLICATION OF ANTERIOR SPINE SURGERY

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Stabilization of the cervical spine is often accomplished via an anterior cervical approach. Bone grafts and/or plates and screws are used to achieve stabilization. Injuries to the pharynx and esophagus are known complications in anterior exposure of the cervical spine. These injuries are manifest in the early postoperative period. Reports of late perforations are very rare. We present four cases of delayed injury to the pharynx and esophagus that resulted in abscess or fistula. We postulate that graft displacement with resulting erosion was responsible for these serious complications. Postoperative odynophagia in patients who undergo anterior cervical fusion warrants evaluation of the bone graft location. Early surgical intervention and repair may decrease prolonged morbidity in these patients.

KEY WORDS — anterior fusion, cervical fusion, cervical spine, pharyngoesophageal perforation.

INTRODUCTION

Patients who sustain flexion injury to the cervical spine with fracture and/or dislocation of cervical vertebrae often require stabilization to prevent further injury of the cervical spinal cord. Definitive surgical intervention most commonly involves an anterior approach to expose the vertebral bodies. Fusion of cervical vertebrae is accomplished by using allograft bone from the iliac crest, which is fashioned into a pocket created in the cervical vertebral bodies. The aim is to reconstruct stable and viable support of the cervical cord.

At Thomas Jefferson University Hospital, a regional spinal cord trauma center, 680 cervical cord injuries were treated between 1979 and 1989. Approximately 60% of these patients underwent surgical stabilization of the spine with anterior fusion. During this time, we have encountered four cases of delayed pharyngocutaneous fistulas. None of these patients sustained perioperative pharyngeal trauma. Our experience with these rare and hazardous complications is presented.

CASE REPORTS

Case 1. This 38-year-old man sustained a C-5 flexion fracture in a diving accident on July 4, 1985. He had an incomplete C-6 spinal cord injury. Cervical tongs were placed, and on July 5, 1985, he underwent anterior cervical fusion from C-4 to C-7 with allograft iliac crest. Sixteen days postoperatively, he developed new-onset odynophagia. Results of a barium swallow study were normal at this time. On July 27, 1985, he developed neck swelling and high fevers. A repeat barium swallow study revealed a pharyngeal fistula present. He underwent immediate neck exploration via the cervical fusion incision and a left paraspinal abscess was drained. The site of pharyngeal perforation could not be demonstrated. A few small pieces of bone that had been displaced from the fusion site and were bathed in the fistula were removed. A Penrose drain was placed and postoperatively he took nothing by mouth (was kept NPO) and had a nasogastric tube in place for feeding. He was treated with intravenous cefoxitin sodium for 14 days on the basis of operating room cultures that grew anaerobes and gram-negative bacteria. He continued to have a salivary fistula that remained stable. Over the next few months he had continued but decreased drainage from the fistula. On November 5, 1985, he was returned to the operating room for drainage of an abscess in the retropharyngeal area. Endoscopy at that time revealed a posterior pharyngeal wall perforation just above the level of the cricopharyngeus muscle. The area appeared to be granulating well and no bone fragments were identified. Over the next 6 weeks, the fistula spontaneously closed. He underwent barium swallow evaluation that confirmed resolution of the fistula in mid-December 1985. He then began oral feeding and experienced no difficulties. A cervical spine computed tomography (CT) scan revealed fibrous fusion and significant resorption of allograft bone. His cervical tongs were removed and he experienced no further difficulties. He currently has had no sequelae from the fistula and remains an incomplete C-6 quadriplegic.

Case 2. This 34-year-old man with a history of insulin-dependent diabetes was involved in a motor vehicle accident September 6, 1984. He sustained a left clavicular fracture, multiple left rib fractures, and a compression fracture at C-7 with incomplete C-7 spinal cord injury. He was stabilized in cervical tongs and transferred to Thomas Jefferson University Hospital. He underwent anterior corpectomy and C-6 to C-7 anterior cervical fusion using allograft iliac crest on October 1, 1984. He had an un-

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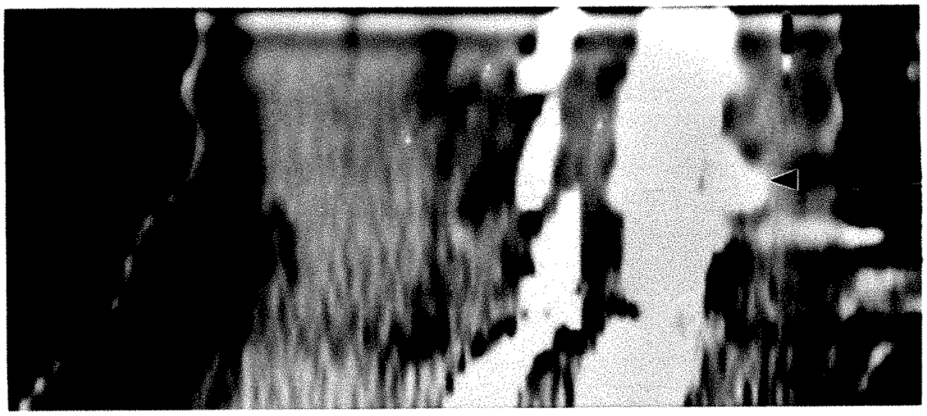

Fig 1. (Case 3) Computed tomographic sagittal reconstruction of cervical spine reveals anteriorly displaced bone fragment (arrowhead) impinging on posterior pharyngeal wall.

eventful early postoperative recovery. In early November 1984 he developed mild odynophagia. Within several days he developed elevated temperatures and white blood cell counts. The left side of his neck became swollen and painful to palpation. A bone scan performed at this time revealed no osteomyelitis in the cervical spine. A gallium scan revealed increased uptake in the soft tissues of the neck. On November 17, 1984, he underwent neck exploration, and an abscess with salivary fistula was discovered in the C-7 area. The perforation was oversewn and drains were placed in the area. He was prescribed intravenous antibiotics on the basis of operating room cultures. He continued to have salivary drainage without cellulitis or abscess in the fistula. He was maintained on gastrostomy feedings and was transferred to the rehabilitation unit in December 1984. The fistula failed to spontaneously close. Follow-up examinations revealed granulation tissue around the fistula site. Barium swallow examinations demonstrated an unchanging fistula tract. Computed tomography scans of the cervical spine revealed failed fusion with resorption of the iliac crest allograft. However, fibrous union was present and he had his cervical halo removed in June 1985. This management continued until July 1985, when he developed elevated temperatures. Workup included a bone scan that revealed possible osteomyelitis of the cervical spine. On July 29, 1985, reexploration of the neck, biopsy of the cervical bone, and debridement of the fistula with oversewing of the esophagus were performed. Bone cultures revealed *Enterobacter* and anaerobic bacteria. He was again placed in cervical traction. He continued to have a draining salivary fistula. On October 4, 1985, he required another neck exploration for drainage of an abscess. Later that month, he underwent a posterior cervical fusion for cervical spine stabilization. He was again maintained on gastrostomy feedings and continued to have drainage until May 1986. The fistula then spontaneously closed and a barium swallow study revealed no leak. He was begun on oral feedings and developed no problems related to the fistula thereafter.

Case 3. This 40-year-old man sustained a C-6 burst fracture that was treated with posterior cervical wiring and anterior cervical fusion November 26, 1986. Postoperatively, he had good recovery until early January 1987, when he developed dysphagia and then right-sided neck swelling with drainage. He had local incision and drainage of the right side of the neck and thereafter was fed with a nasogastric tube and kept NPO. He was given intravenous antibiotics as dictated by cultures for 14 days. The drainage cleared and he developed a noninfected salivary fistula. He had a percutaneous gastrostomy placed and was kept NPO. Fiberoptic laryngoscopy revealed a dysfunction of the right superior laryngeal nerve. He was maintained in cervical halo traction over the next few months and had a persistent cervical fistula without abscess or cellulitis. Barium swallow evaluation on repeated occasions failed to reveal esophageal leakage, but there was preferential filling of the left pyriform sinus. However, he required two additional cervical drainage procedures for abscess, in March and April 1987. A CT evaluation of his cervical spine revealed fibrous union of his spine, and halo traction was removed in April 1987. He continued to have cervical drainage. He was readmitted on October 27, 1987, and had a CT of the neck and cervical spine, revealing significant resorption of iliac crest bone with a bony fragment displaced anteriorly at the inferior site (Fig 1). He underwent direct laryngoscopy on November 2, 1987, and a large amount of granulation tissue was found in the right pyriform sinus. There appeared to be a small punctate rent in the apex of the right pyriform sinus mucosa. The neck was explored along the fistula tract and a sequestrum of osteomyelitic bone was found and removed. The cervical drainage stopped after operation and results of a follow-up barium swallow study on November 11, 1987, were reported to be normal. The patient was begun on oral feeding and has developed no complications since that time.

Case 4. This 68-year-old man saw a neurosurgeon for complaints of upper extremity paresthesia and weakness. Evaluation and CT revealed severe cervical spondylosis with anterior compression. He underwent anterior cervical fusion from C-3 to C-7 on October 19, 1988. Postoperatively he did well and was discharged home in cervical tongs. He pre-

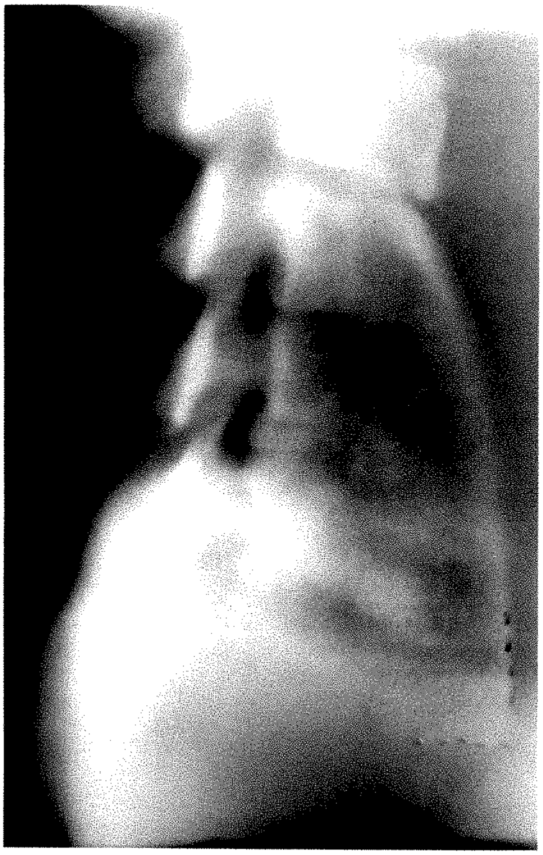

Fig 2. (Case 4) Lateral cervical tomogram reveals anterior-inferior displacement of iliac crest allograft.

sented to the Thomas Jefferson University Hospital emergency room complaining of difficulty swallowing and fever on November 29, 1988. Lateral cervical spine x-ray films revealed anterior displacement of the spinal fusion graft (Fig 2); a barium swallow study done at this time showed no leak. He was brought to the operating room December 1, 1988, and some purulent material was found in the area of the anteriorly displaced graft. The area was irrigated after cultures were taken and the wound was closed. The patient continued to have fever and developed salivary drainage on the first postoperative day. Methylene blue was given orally and confirmed the presence of a pharyngocutaneous fistula. A gastrograffin swallow study confirmed the fistula, but the exact level of the fistula could not be determined. He was returned to the operating room December 5, 1988, and upon exploration of the neck was found to have a 1-cm posterior esophageal perforation at the C-7 level, at which the inferior portion of the iliac crest allograft was anteriorly displaced. The tissues around the perforation were markedly inflamed and edematous. A two-layer closure of the perforation was attempted. The iliac crest bone graft was removed. Two large suction drains were placed and the skin was loosely approximated. He was maintained in cervical tongs for spine stabilization. A feeding gastrostomy was placed. On the third postoperative day, he developed some salivary drainage in his suction drains. He had compression dressings placed and was kept NPO. He was maintained on intravenous penicillin on the basis of operating room cultures that grew α-hemolytic streptococci. The drainage spontaneously stopped by December 23, 1988. A repeat barium swallow study on December 28, 1988, revealed no fistula, but a small posterior pharyngeal irregularity. Fiberoptic pharyngoscopy failed to reveal any abnormalities. He was maintained on gastrostomy tube feedings until January 16, 1989. He underwent a repeat barium swallow study; the findings were normal. He underwent a posterior approach to the cervical spine and had a successful cervical fusion on February 11, 1989. His cervical tongs were removed 6 weeks later and he now is in good condition with no further complications.

DISCUSSION

Pharyngoesophageal injury after anterior spinal fusion procedures has been described since the development of the procedure. Almost all reports involve fistulas developing in the early postoperative period. Delayed fistulas are rare and most likely have a different cause. In each of the previously described cases, patients developed cervical fistulas several weeks to months after anterior spinal fusion. All had recovered from the early postoperative period and were tolerating solid diets without pharyngeal complaints.

Pharyngeal complications after cervical spine injury have been reported. Morrison[1] described a case in which a posterior esophageal tear appeared to be caused by the exposed C-7 vertebral body in a patient with C6-7 subluxation and an anterior longitudinal ligament tear. Tomaszek and Rosner[2] reported two cases involving fracture dislocations in the C6-7 region with esophageal injury. One patient developed neck abscess, the other mediastinitis and empyema. These reports demonstrate pharyngoesophageal injury with isolated cervical spine trauma. Other reports of esophageal injury in blunt trauma are related to increased intraesophageal pressure with rupture in the cricopharyngeus region.

Intraoperative injury to the pharynx during anterior spinal fusion is rare. Experience with the procedure since the 1950s has produced a safer operative technique. Gentle dissection and retraction of the pharynx and esophagus avoids direct trauma. Corpectomy and graft placement as described by Rothman and Simeone[3] and Bohlman and Eismont[4] eliminates foreign materials, such as wires, that have produced esophageal injuries. The technique involves creation of a pocket to accept an appropriately fashioned iliac crest allograft while the spine is in extended traction. Small fragments of allograft bone are placed to fill the corpectomy site. Care is taken not to leave rough surfaces along the anterior

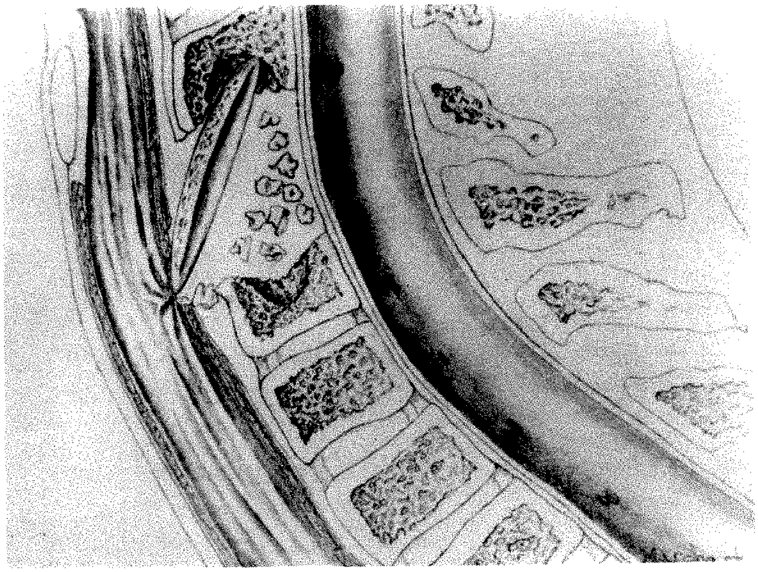

Fig 3. Artist's depiction of sagittal view of anterior-inferior graft displacement with impingement on posterior pharyngeal wall. Iliac crest allograft has been resorbed, allowing for anterior displacement.

surface of the fusion site. Neither Cloward[5] nor Tew and Mayfield[6] reported any cases of intraoperative pharyngoesophageal injury in several hundred anterior spinal fusions. At Jefferson, we have seen no early pharyngeal perforations from intraoperative trauma in about 350 cases.

Delayed injury to the pharynx and esophagus after anterior spine surgery has been reported. Whitehill et al[7] and Kuriloff et al[8] each reported a case of delayed fistula after cervical spine fusion occurring 6 to 10 weeks after operation. In one case, anterior displacement of an iliac crest graft was demonstrated on radiographs.

In our series of patients, all developed odynophagia as the first symptom. In three of the four cases, fever and neck swelling occurred more than 24 hours after the swallowing difficulty. The fourth patient presented to the emergency room with odynophagia of 2 days' duration and new-onset fever. These findings suggest that the patients sensed the displacement of the iliac crest graft or surrounding bone fragments just prior to perforation. One patient underwent lateral cervical spine radiographs and tomograms demonstrating the graft displacement (case 4). Dysphagia after anterior spine surgery has been reported[9] and may be related to perioperative swelling or hematoma. However, odynophagia after spinal fusion is rare and probably warrants evaluation of the fusion site.

Contrast pharyngoesophagrams were diagnostic after perforation occurred. However, in cases 1 and 4, barium swallow studies performed at the presentation of odynophagia did not reveal perforations. Once these patients developed neck swelling, however, all contrast studies were positive. Contrast swallowing studies are recommended to aid in determining location of the perforation and possible extension of extravasation. However, negative results should not decrease suspicion of impending or developing perforation.

Computed tomography scans were performed in three patients. These scans may help delineate the extent of abscess and possible extension along the prevertebral space and therefore should be performed if possible. Evaluation of the iliac crest allograft position in the sagittal plane is most easily accomplished with cervical tomography. In case 4, cervical tomograms clearly demonstrated graft displacement. Sagittal reconstruction of CT scans as in case 3 could also be useful in evaluating bone displacement or bony fragments impinging on the pharynx.

Bone scans were performed in two patients. In one case, osteomyelitis was suspected. Bone scanning of cervical fusion sites will reveal increased uptake for about 9 months after operation. This is related to remodeling and osteointegration of the living iliac crest graft. Infection in a viable graft would display markedly increased uptake. Confusion may thus occur if portions of the allograft are nonviable and serve as infected foreign bodies. These areas will not show markedly increased activity.

Operative considerations in these cases center upon adequate drainage of abscess and drain placement. If bony fragments or the iliac crest graft are exposed to infection, they must be removed. Dissection along the planes of previous exposure and/or along the fistula tract avoids spread of infected material in fresh tissue planes. In the first three cases, the iliac bone grafts did not appear to be directly involved in the abscess and were not removed. There appeared to be a fibrous barrier over the grafts. However, these patients had prolonged fistulas, most likely secondary to low-grade infection associated with the graft, which acted as a foreign body in the fistula area. In the fourth case, the graft was removed and the fistula closed quickly.

Evaluations of the first three patients revealed failed graft fusions with major resorption of the iliac crest grafts. These patients developed secondary firm fibrosis in the corpectomy sites that provided adequate stabilization of the spine and allowed external stabilization to be discontinued. This process took months to over a year to occur. In the fourth case, the patient underwent a posterior approach and fusion and had external stabilization removed 4 months after he initially developed his fistula. At the time of his graft removal, 41 days after anterior spinal fusion, the graft had resorbed and was several millimeters smaller than the anterior lip of the corpectomy site (Fig 3). Closure of the pharynx or esophagus is recommended if possible, with consideration of reinforcement with muscle flap if necessary.[10]

The fate of iliac crest allografts in cervical fusion is not certain. Almost all grafts undergo some resorption after placement, although successful fusion is almost always accomplished. Some degree of anterior graft displacement is not rare, and fibrous union is considered acceptable. It appears that this anterior displacement of the iliac crest allograft with surrounding bone chips is responsible for these rare cases of delayed pharyngoesophageal perforation.

CONCLUSION

Delayed pharyngoesophageal perforation after anterior spinal fusion is a rare complication. All patients presented with odynophagia. Perforations were located at the inferior portion of the fusion site. Anterior displacement of the graft with erosion into the esophagus was the most likely cause. Adequate drainage and removal of infected bone is essential in managing these potentially life-threatening complications.

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ITALIAN EXPERIENCE OF VOICE RESTORATION AFTER LARYNGECTOMY WITH TRACHEOESOPHAGEAL PUNCTURE

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This report concerns 102 cases of tracheoesophageal puncture performed as a means of secondary voice restoration after total laryngectomy, in 70 patients proving unable to learn esophageal speech and as a treatment of choice in a further 32 cases. Complications arose in 21 cases but were generally minor and could be overcome. Results were favorable in 45 of 70 and 29 of 32 cases, respectively. The method was considered effective, particularly when supported by the patient's determination to learn a verbal communication method.

KEY WORDS — prosthesis, total laryngectomy, tracheoesophageal puncture, voice restoration.

INTRODUCTION

Voice restoration after total laryngectomy has represented one of the major problems facing the laryngeal surgeon and speech pathologist. Esophageal speech, the artificial larynx, and various surgical procedures are frequently used, but are far from trouble-free. Singer and Blom[1] have reported favorable results with a valved silicone prosthesis inserted in a tracheoesophageal fistula. This endoscopic technique is relatively straightforward and enables an effective control of aspiration. In 1985, Hamaker et al[2] used this method simultaneously with total laryngectomy. Satisfactory results with primary and secondary tracheoesophageal puncture have been confirmed by various authors.[3-8]

This is a report of our experience using the secondary tracheoesophageal puncture technique, with a discussion of results obtained with this method both as an alternative for patients unable to use esophageal speech and as a rehabilitative treatment of choice.

MATERIALS AND METHODS

Between 1982 and 1989, a total of 102 patients underwent tracheoesophageal puncture for voice restoration at the otolaryngology department of San Bortolo Hospital in Vicenza. These patients may be considered in two separate groups.

Group 1. The first group includes 70 patients unable to learn esophageal speech, ie, 65 men and 5 women 35 to 78 years of age (mean age, 59.8 years). The interval between total laryngectomy and prosthesis implant varied from 2 months to 21 years. Prior to tracheoesophageal puncture, patients had undergone total laryngectomy (50 cases), total laryngectomy with unilateral or bilateral neck dissection (14 cases), or total laryngectomy with partial or subtotal hypopharyngectomy (6 cases, 4 of which were reconstructed with a deltopectoral skin flap and 2 with a pectoralis major myocutaneous flap). Preoperative or postoperative radiotherapy had been provided in 37 cases. Partial laryngectomy had previously been performed in 35 of our patients.

Patients were selected on the basis of their motivation to learn a means of verbal communication. They all underwent a preoperative barium swallow study, pharyngoesophageal radiography, and an esophageal insufflation test, first with a urethral catheter and a 50-mL syringe and subsequently by an adaptation of the method described by Blom et al[9] that uses the patient's own breathing apparatus.

Creation of the tracheoesophageal fistula was performed according to the method described by Singer and Blom[1] in all cases. Tracheoesophageal puncture was associated with pharyngeal constrictor myotomy in two patients. The catheter was usually replaced by the prosthesis 48 hours after operation. The patient was then trained in the use and maintenance of the fistula and prosthesis. The tracheostoma valve was used for entraining air from the airway to the digestive tract in selected cases. Hospitalization generally lasted from 4 to 7 days.

Group 2. Since 1989, our team has used tracheoesophageal puncture as the rehabilitative method of choice for a total of 74 patients. Of these, 42 cases are too recent for our evaluation of results at present; the remaining 32 were considered as a second group (29 men and 3 women between 43 and 80 years of age; mean age, 60.8 years). Previous operations had involved total laryngectomy (17 cases), total laryngectomy with unilateral or bilateral neck dissection (12 cases), and total laryngectomy with partial or subtotal hypopharyngectomy (3 cases, 1

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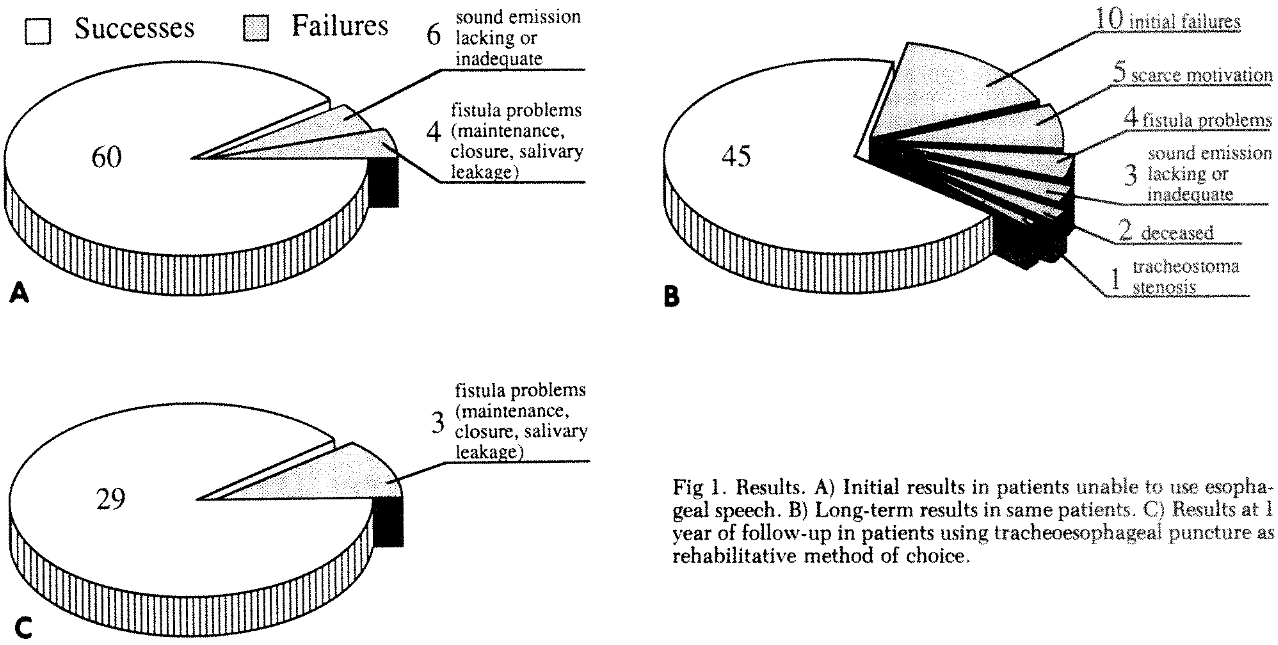

Fig 1. Results. A) Initial results in patients unable to use esophageal speech. B) Long-term results in same patients. C) Results at 1 year of follow-up in patients using tracheoesophageal puncture as rehabilitative method of choice.

of which involved reconstruction with a deltopectoral skin flap, 1 with a pectoralis major myocutaneous flap, and 1 with a cutaneous revascularized graft). Preoperative or postoperative radiotherapy had been provided in 15 cases. Six patients had previously undergone partial laryngectomy. Particular care was taken with certain aspects of the total laryngectomy in the majority of group 2 patients, as cutaneous incision, stoma construction, pharyngeal constrictor myotomy, and hypopharyngeal closure are fundamental steps in the success of the voice prosthesis.

Overall, the Blom-Singer normal and low-pressure voice prostheses were the most frequently used; only three patients were fitted with the Colorado prosthesis. The low-pressure or normal voice prosthesis was used with a suitably fenestrated silicone tracheostoma vent in nine cases.

RESULTS

Group 1. Sixty of the 70 patients (86%) quickly acquired an intelligible voice with the prosthesis. Of the 10 unsuccessful cases (Fig 1A), sound emission was lacking or inadequate in 6 patients, who refused pharyngeal myotomy, and problems arose concerning the fistula in 4 cases, including closure, liquid aspiration, and prosthesis-insertion problems. Over a year later, only 45 patients of the 70 (64%) were still using the prosthesis (Fig 1B). Of the 15 cases proving unsuccessful in the long term, the main reason for failure was inadequate motivation to learn a verbal communication method (particularly in 5 patients who had been laryngectomized for many years). Four patients gave up using the prosthesis owing to problems concerning the fistula (maintenance, closure, salivary leakage). Another 3 patients considered the quality of the tracheoesophageal speech unacceptable. Progressive shrinking of the tracheostoma obliged 1 patient to remove the prosthesis. Two patients died of cancer less than a year after implanting the prosthesis. Only 8 patients were continuing to use the tracheostoma valve instead of manual closure.

Group 2. After 1 year of follow-up, results were favorable in 29 of the 32 cases (91%) (Fig 1C). These patients found it easier than group 1 patients to produce sounds, owing to less resistance from the pharyngoesophageal segment. The tracheostoma valve was also being used more (by 14 of 29 patients).

Among the 28 unsuccessful cases in groups 1 and 2, spontaneous closure of the fistula took place in all but 4 patients: 3 required an injection of sclerotizing substances in the fistula walls, and 1 needed surgical closure.

COMPLICATIONS AND THEIR TREATMENT

One or more complications arose in 21 of the 102 patients, all of which concerned the creation and maintenance of the tracheoesophageal fistula. The incidence and type of complications are summarized in the Table. Peristomal and cervical cellulitis and tracheobronchial infections occurred in 3 patients postoperatively and needed a prolonged antibiotic treatment. There was necrosis of the soft tissue around the fistula in 2 patients who had previously undergone radiotherapy. A lengthy hospitalization was required owing to spontaneous fistula closure in 1 case and to fistula shrinking in another (with subsequent reapplication of the prosthesis). Fistula incontinence with salivary leakage around the prosthesis occurred in 5 patients, who were treated with silver nitrate cauterization (2 cases), prosthesis replacement with a more suitable model (2 cases), or injection of sclerotizing substances in the fistula

COMPLICATIONS IN 21 PATIENTS

Type of Complication	*No. of Cases*
Tracheobronchial inflammation	2
Peristomal and cervical cellulitis	1
Necrosis of fistula walls	2
Salivary leakage	5
Closure of fistula	4
Granulation tissue	4
Aspiration of prosthesis	2
Formation of false tract	1
Fistula migration	1
Tracheostoma stenosis	1
Aerophagy	1

wall (1 case). Four cases presented granulation tissue around the outer fistula orifice (Fig 2A) and this was removed with electrocautery. In histologic terms, this was a granulation tissue rich in newly formed blood vessels (Fig 2B). An experimental prosthesis coated with a thin film of pyrolytic carbon (a biocompatible material) was therefore fitted in these patients (Fig 2C). Fiberoptic bronchoscopy was performed in 2 cases to remove a prosthesis that had been sucked into the main right bronchus. Closure of the fistula, formation of a false tract, prosthesis aspiration, and fistula migration made tracheoesophageal repuncture necessary in 6 patients. This was done by the normal procedure in 1 case; in 5 cases it was performed under local anesthesia with an angiographic catheter and a suitably adapted urethral catheter (Fig 3). One patient presenting stenosis of the tracheostoma preferred to remove the prosthesis rather than try the Colorado model or a Blom-Singer prosthesis with a fenestrated tracheostoma vent. Nonetheless, 14 of the 21 patients who suffered complications have continued to use the prosthesis.

DISCUSSION

Most laryngectomized patients are rehabilitated to use esophageal speech, although many are incapable of learning this method adequately.[10,11] In the last 10 years, surgical approaches to voice rehabilitation have made considerable progress with the advent of the tracheoesophageal puncture technique developed by Singer and Blom.[1] In the United States, voice prostheses have become popular with head and neck surgeons and form a significant proportion of voice rehabilitation procedures.[12] Interest in the new technique is confirmed by the number of new prostheses on the market,[13-18] although none seem to offer significant advantages over the normal and low-pressure Blom-Singer models.

The fistula for the prosthesis can be prepared ei-

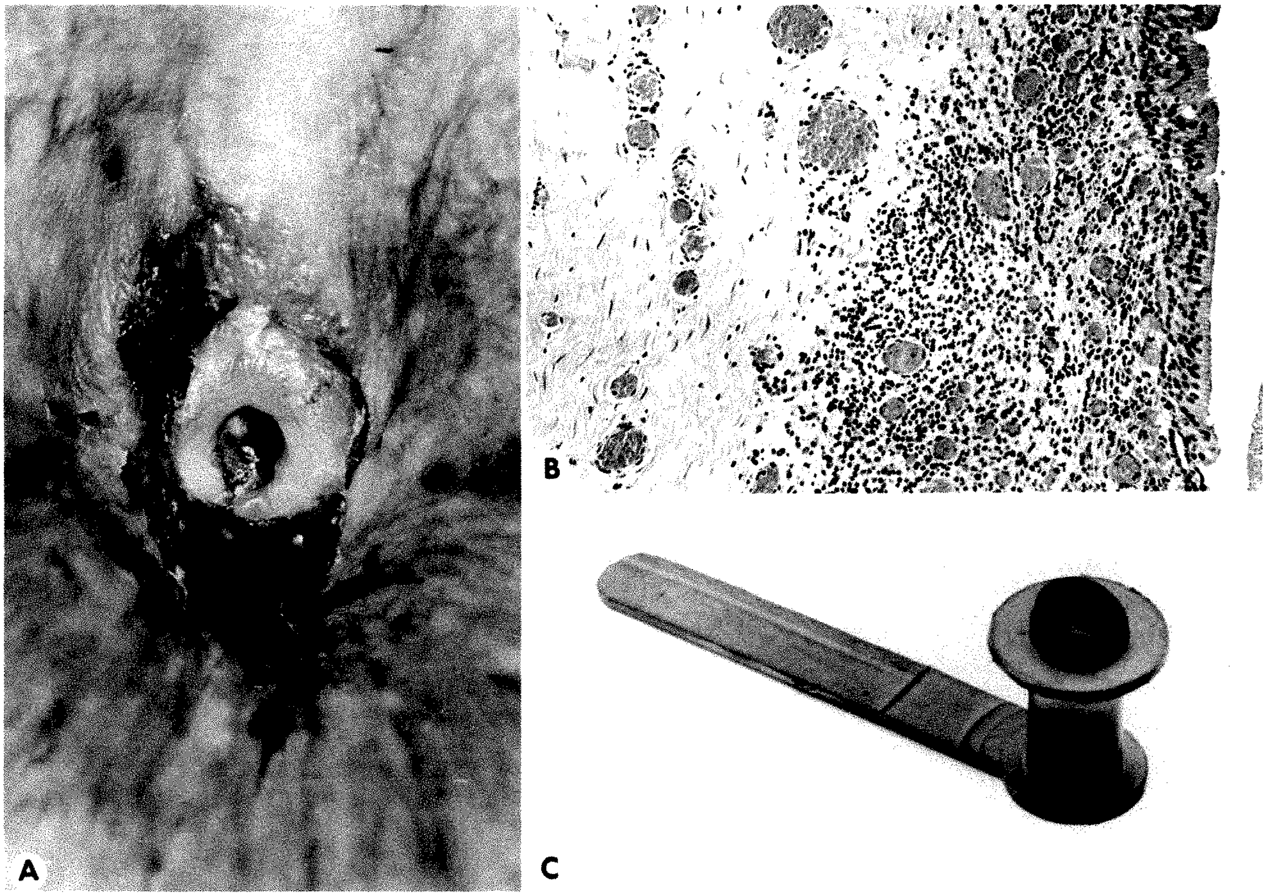

Fig 2. Granulation tissue and treatment device. A) Granulation tissue around tracheoesophageal fistula orifice. B) Histologically, lesion presents granulation tissue rich in newly formed blood vessels (H & E, original x40). C) Experimental prosthesis with pyrolytic carbon coating.

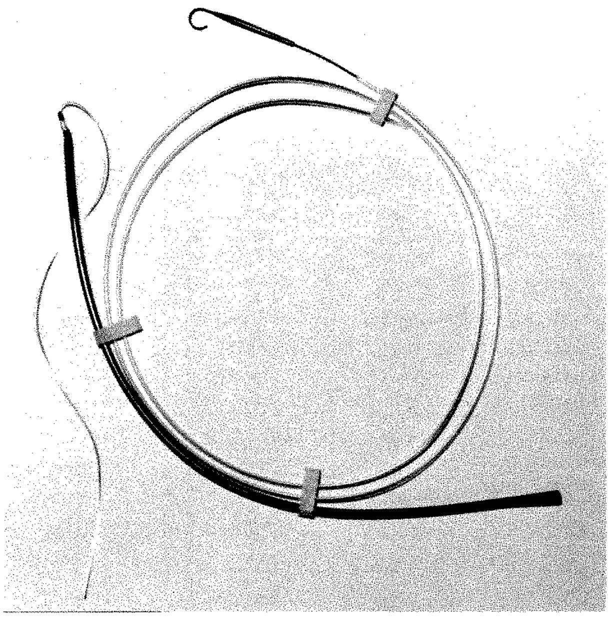

Fig 3. Angiographic catheter and urethral catheter used for repuncture under local anesthesia.

ther during total laryngectomy (primary rehabilitation) or at a later date (secondary rehabilitation), and there is some debate as to which solution offers the best results.[7,19-22] As of 1982, secondary tracheoesophageal puncture was performed in 70 patients who had been unable to learn esophageal speech. Results were initially favorable in 86% of cases and still positive in 64% after 1 year of follow-up (considered a sufficient interval for final evaluation[6,23]). Initial failures were generally due to hypertonicity of the pharyngoesophageal tract and problems with the use and maintenance of the fistula and prosthesis. Inadequate motivation was the most influential negative factor in the long term.

As of 1989, our team adopted the tracheoesophageal puncture technique as the rehabilitative method of choice; hence, patients were prepared for operation and the rehabilitation program with suitable psychological support. Without neglecting accepted oncologic procedures, the total laryngectomy was altered to accommodate the tracheoesophageal puncture. It is important to establish a sufficiently ample tracheostoma that is not embedded behind the sternum and also to perform a pharyngeal constrictor myotomy. The pharyngoesophageal spasm that sometimes prevents patients from acquiring an adequate voice may be overcome either by myotomy of the cricopharyngeal and pharyngeal constrictor muscles[24] or by pharyngeal plexus neurectomy.[25] The only drawback observed, also reported by Mahieu et al,[26] was aphonia in two myotomized patients due to excessive hypotonicity of the pharyngeal tract. External manual pressure to the pharynx may improve the quality of speech. Olson and Callaway[27] have suggested not suturing the pharyngeal constrictors across the closure of the pharynx as an alternative to myotomy or plexus neurectomy.

Of the patients thus treated to date, results have proved favorable in 91% of the 32 cases with adequate follow-up (1 year). The smoother peritracheostomal surface and a reduced resistance in the pharyngoesophageal tract enable the tracheostomal valve to be used more frequently.

The technique is not entirely trouble-free and problems can stem from the endoscopic instruments or from the tracheoesophageal fistula creation and maintenance. According to the literature, complications have an incidence varying from 15% to 25%[28,29] and include esophageal perforation, cervical spine fracture, osteomyelitis of the vertebrae, peristomal and cervical cellulitis, mediastinitis, aspiration, pneumonia, enlarging fistula with salivary leakage, aspiration of the prosthesis, stoma stenosis, esophagus stenosis, false tract formation, fistula migration, and allergic reaction to the prosthesis. A pneumothorax has also been reported[30] as a complication due to the use of a voice prosthesis. Granulation tissue can form around the orifice of the fistula in reaction to the foreign body.[20,31,32] The complications observed by our team were similar to those described elsewhere in the literature, although no severe problems were caused by the esophagoscopic instruments. The onset of complications did not necessarily mean abandoning the prosthesis, and sufficiently motivated patients proved able to overcome most of these problems, which were generally of a modest extent.

Voice restoration with tracheoesophageal puncture is not only relatively straightforward, it also has the advantage of placing no restrictions on oncologic therapy. Radiotherapy can be used both before and after the prosthesis implant.[29,33] Very extensive operations, with reconstruction of the hypopharynx and cervical esophagus with a deltopectoral skin flap, myocutaneous flaps, a cutaneous revascularized graft, and transposition of the viscera, does not preclude this type of rehabilitation, and favorable results have been reported by various authors.[34-36]

The tracheoesophageal puncture technique is an effective method for voice restoration after total laryngectomy even in patients who have failed to learn other forms of speech, especially if the abilities of surgeons and speech therapists are supported by the patient's determination to learn a verbal communication method.

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EXPRESSION OF INTERMEDIATE FILAMENT PROTEINS IN THE ADULT HUMAN COCHLEA

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The immunohistochemical localization of intermediate filament proteins was studied in frozen sections of chemically fixed, nondecalcified adult human cochleas. Cytokeratins were found in all epithelial cells lining the cochlear duct (including most supporting cells of the organ of Corti) but were absent in the hair cells. Neurofilament proteins were present in the nerve endings at the hair cells, in the neural bundles, and in the ganglion cells. Vimentin staining occurred in most of the supporting structures and was roughly complementary to the regions showing cytokeratin staining and neurofilament staining. However, the region of the spiral prominence and outer sulcus, as well as the pillar cells and Deiters' cells in the organ of Corti, showed coexpression of vimentin and cytokeratins. No definite immunostaining was observed with antibodies to desmin and glial fibrillary acidic protein.

KEY WORDS — adult human cochlea, immunohistochemistry, intermediate filament proteins.

INTRODUCTION

Intermediate filaments (IFs) are part of the cytoskeleton of eukaryotic cells and form a class of highly insoluble cytoplasmic filaments. These filaments are intermediate in size between the other two main constituents of the cytoskeleton, ie, microtubules and microfilaments. Biochemically, they can be grouped into five major classes: desmin (55 kd) is expressed by muscle cells; vimentin (57 kd) by mesenchymally derived cells; cytokeratins (40 to 68 kd) by epithelial cells; neurofilament proteins (68, 150, 200 kd) by cells of neuronal differentiation; and glial fibrillary acidic protein (GFAP; 52 kd) by astroglia and related cells.

This cell type specificity of IFs is of particular value in studies on histogenesis, as a given tissue can be characterized by its distribution of IFs.[1,2] However, it has become clear that there are exceptions to this general classification system. A few epithelioid tissues have been found not to contain cytokeratins but to express vimentin, and it has also been shown that some specialized cell types can coexpress up to three different IF proteins under certain circumstances.[3] Furthermore, it has become clear that certain tissue types in developing embryos may contain IF proteins different from those present in their adult counterparts.[4]

In the past decade virtually all kinds of human tissues have been investigated for their expression of IF proteins. The cochlea, however, was not studied in this respect until Flock et al[5] first described the presence of prekeratin (ie, cytokeratin) in the supporting cells of the guinea pig organ of Corti. Since then, only a few studies have been published on the distribution of one, several, or all five of the IF proteins in the cochlea.[6-14] Moreover, until recently only animal species had been investigated, and data on the adult human cochlea are still lacking.

Shi and Juhn[6] localized keratin in the cochlear duct of the guinea pig by means of an indirect immunoperoxidase technique on aldehyde-fixed, resin-embedded tissue. Anniko et al[7] found vimentin and neurofilament proteins, but no cytokeratins, desmin, or GFAP in the newborn inner ear of the mouse using immunofluorescence on unfixed, frozen sections. In contrast, using an indirect immunoperoxidase technique on unfixed, frozen tissue, Anniko et al[8,9] did find cytokeratins in the cochlear duct of 14- to 18-week-old human fetuses, in addition to vimentin and neurofilament proteins. This was confirmed by other studies — one on human fetal cochleas[10] and others on the mouse inner ear[11,12] — using, respectively, immunofluorescence and indirect immunoperoxidase staining of frozen sections. Kasper et al[13] described the expression of vimentin and cytokeratins in the stria vascularis of unfixed, decalcified, cryosectioned guinea pig cochleas. Finally, Schrott et al[14] studied the expression of IFs in aldehyde-fixed, decalcified, paraffin-embedded sections of cochleas of normal and mutant mice. However, desmin and GFAP reactivity could

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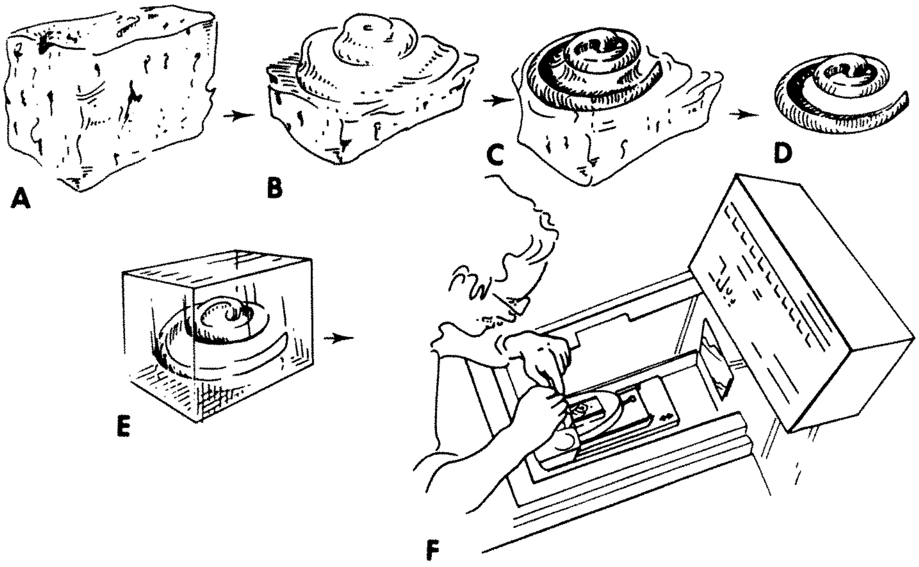

Fig 1. Temporal bone processing procedure. A) Temporal bone after removal at autopsy. B) Bony labyrinth after drilling procedure. C) After removal of otic capsule, membranous labyrinth is visible. D) Membranous labyrinth removed in toto. E) Embedding in Tissue-Tek II. F) Cryosectioning.

not be defined, because only the polyclonal antibodies to cytokeratins and vimentin and the monoclonal antibody to neurofilament proteins appeared to be reactive on the paraffin sections. Cytokeratin and vimentin staining were found in the cochlear duct, whereas neurofilament staining was confined to a few scattered cells in the spiral ganglion.[14]

The small number of studies on IF protein expression in the cochlea, the partly conflicting data, and the absence of data on the adult human cochlea may all be explained by technical difficulties encountered in inner ear immunohistochemistry. Because of the delicate structure of the membranous labyrinth and the surrounding bone of the otic capsule, the immunoreactivity-compromising steps of both decalcification and paraffin or resin embedding prior to sectioning are generally regarded to be inevitable. Immunohistochemistry of the adult human cochlea offers additional problems, because chemical fixation cannot be avoided and the heavily calcified temporal bone necessitates prolonged decalcification.[15,16] However, it has been well established that in immunohistochemical localization of IF proteins, conventional formaldehyde fixation combined with paraffin embedding may lead to weak or even false-negative staining results. The most reliable results are obtained by using frozen sections and, when fixation is necessary, by using protein-precipitating fixatives.[1,17,18]

Recently, we developed a new procedure that enabled us to investigate frozen sections of chemically fixed, nondecalcified adult human cochleas, thus preserving optimal antigenicity.[16] The aim of the present study was to analyze the expression patterns of IF proteins in the adult human cochlea by use of this new procedure.

MATERIAL AND METHODS

Tissue Processing. Temporal bones ($n = 12$) of six human adults, 32 to 73 years of age, without any known history of hearing impairment were fixed within 3 hours after death by perilymphatic perfusion with acetone (100%) for 10 minutes followed by perfusion with phosphate-buffered saline (PBS). After removal at autopsy, the temporal bones were immediately microdissected, essentially as described by Hawkins and Johnsson.[19] Osmium tetroxide postfixation was omitted because of its known deleterious effects on immunoreactivity. In order to maintain the tissue in optimal condition and to prevent drying of the membranous labyrinth, the entire procedure was performed in cold PBS (4°C). After removal of the otic capsule, the membranous labyrinth was detached from the modiolus by cutting through the osseous spiral lamina. Next, the membranous labyrinth was removed in toto from the remnants of the bony capsule, followed by embedding in Tissue-Tek II and cryosectioning (4 to 5 μm) (Figs 1 and 2).

Antisera. Sections were incubated with polyclonal rabbit and monoclonal mouse antibodies to all five main classes of IF proteins, ie, cytokeratins, vimentin, neurofilament proteins, desmin, and GFAP,

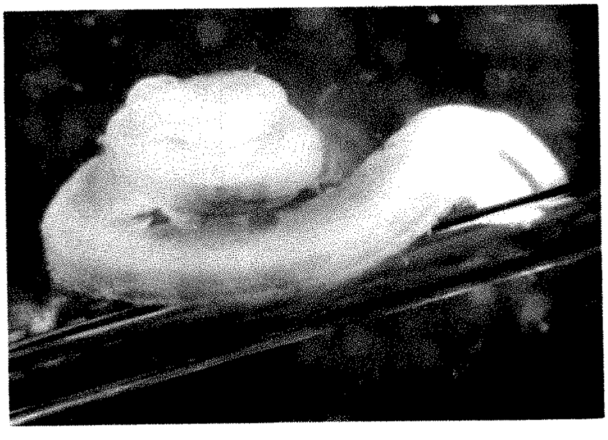

Fig 2. Membranous labyrinth, after microdissection and subsequent removal in toto from remnants of bony capsule.

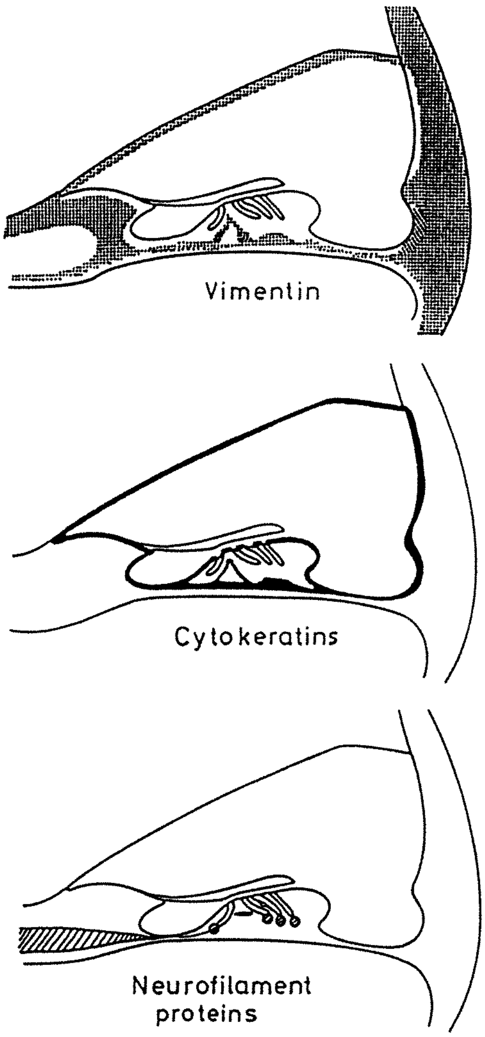

Fig 3. Schematic representation of immunostaining for vimentin, cytokeratins, and neurofilament proteins in cochlear duct.

most of which were obtained from Euro-Diagnostics BV, Apeldoorn, the Netherlands. Cytokeratins were detected with the affinity-purified polyclonal rabbit antibody PKE (dilutions 1:25 to 1:100) and with the broad-spectrum monoclonal antibody RCK 102 (dilutions 1:2.5 to 1:5; reacting with virtually all epithelial tissues). Vimentin was detected with the affinity-purified polyclonal rabbit antibody PVI (dilutions 1:700 to 1:1,400) and with the monoclonal antibody RV 202 (dilutions 1:200 to 1:600).[20] For detection of the neurofilament proteins three monoclonal antibodies were used, ie, MNF (dilutions 1:10 to 1:20; directed to the 68- and 200-kd subunits) and RNF 401 and RNF 402 (dilutions 1:1 to 1:5 and 1:5 to 1:20; directed to the 200-kd subunit).[21] For detection of desmin and GFAP, polyclonal and monoclonal antibodies to desmin (PDE, dilutions 1:150 to 1:300; MDE, dilutions 1:1 to 1:2.5) and GFAP (PGF, dilutions 1:400 to 1:800; MGF, dilutions 1:1 to 1:1.5) were used.

Immunolabeling. Frozen sections (4 to 5 μm thick) were air-dried at room temperature (15 minutes), fixed in 100% acetone (3 minutes), and air-dried once more. After washing in PBS the specimens were incubated with 10% normal goat serum (NGS) (X 902, Dakopatts Corp, Denmark) in PBS for 20 minutes in order to diminish nonspecific binding. The sections were then incubated with the primary antibodies at the appropriate dilutions in 10% NGS for 30 minutes. After washing in PBS, the sections were incubated with the secondary antibody — rabbit anti mouse peroxidase (P 260 Dakopatts Corp) for monoclonal antibodies or swine anti rabbit peroxidase (P 217 Dakopatts Corp) for polyclonal antibodies — in 10% NGS for another 30 minutes. 3-Amino-9-ethylcarbazole served as a chromogen for the peroxidase reaction. Finally, sections were counterstained with Mayer's hemalum, mounted in Kaiser's glycerol gelatin, and examined by light microscopy.

Appropriate human positive control tissues were included to prove the specificity of the used antibodies. Negative controls were obtained by replacement of the primary antibody by either PBS or tissue culture medium (RPMI 1640, 10% FCS).

RESULTS

All positive controls showed specific staining, thus proving the reactivity of the antibodies. Immunostaining for the different antisera yielded similar results in all temporal bones, differing only in the degree of staining. The overall staining pattern throughout the cochlear duct is depicted in Fig 3 and summarized in the Table.

Cytokeratins. Immunostaining with the polyclonal and monoclonal antibodies to cytokeratins occurred in all epithelial cells lining the endolymphatic space of the membranous labyrinth. This includes Claudius' cells, the outer sulcus cells, the spiral prominence (especially those cells adjacent to the stria vascularis), the marginal cells of the stria vascularis, Reissner's membrane (probably only the epithelial cells), the interdental cells, the inner sulcus cells, and the organ of Corti (Figs 4-6).

In the organ of Corti staining was present in the border cells, the inner and outer pillar cells, Deiters' cells, and Hensen's cells. Intense staining occurred at the appositions of these cells to the basilar membrane and along the surface of the organ of Corti, to which region all these cells contribute (ie, reticular lamina). No staining, however, occurred in the hair cells (Fig 4B).

Vimentin. The polyclonal and monoclonal antibodies gave identical results. Immunostaining occurred in most supporting structures of the membranous labyrinth (Fig 4C). The spiral ligament stained positive for vimentin. In the stria vascularis both intermediate and basal cells showed vimentin staining, while staining of the marginal cells seemed

STAINING PATTERN FOR ALL FIVE INTERMEDIATE FILAMENT PROTEINS THROUGHOUT COCHLEAR DUCT

	Cytokeratins	*Vimentin*	*Neurofilament Proteins*	*GFAP*	*Desmin*
Reissner's membrane	+	+	−	−	−
Basilar membrane					
Mesothelial lining	−	+	−	−	−
Amorphous part	−	−	−	−	−
Nerve fibers	−	−	+	±*	−
Interdental cells	+	−	−	−	−
Spiral limbus	−	+	−	−	−
Inner sulcus cells	+	−	−	−	−
Organ of Corti					
Border cells	+	−	−	−	−
Deiters' cells	+	+	−	−	−
Hair cells	−	−	−	−	−
Pillar cells	+	+	−	−	−
Hensen's cells	+	−	−	−	−
Tectorial membrane	−	−	−	−	−
Claudius' cells	+	−	−	−	−
Outer sulcus cells	+	+	−	−	−
Spiral prominence					
Epithelial cells	+	+	−	−	−
Stroma	−	+	−	±*	−
Stria vascularis					
Marginal cells	+	−?	−	−	−
Intermediate and basal cells	−	+	−	−	−
Spiral ligament	−	+	−	−	−

GFAP — glial fibrillary acidic protein.

*Questionable reaction only with polyclonal antiserum.

negative. Both the epithelial lining and the stroma of the spiral prominence showed positive immunostaining, as did Reissner's membrane (probably only the mesothelial cells). In the organ of Corti staining was limited to the inner and outer pillar cells and Deiters' cells (Fig 4D). Other cells of the organ of Corti showed no immunoreactivity. Also, Claudius' cells, the inner sulcus cells, the region of the interdental cells, and the region of the neural bundles lacked reactivity for vimentin (Fig 4C).

Neurofilament. All antibodies to the neurofilament proteins revealed identical staining results. Immunostaining occurred in the neural bundles reaching the organ of Corti (Fig 4E). In the organ of Corti, nerve fibers and nerve endings at inner and outer hair cells stained intensely (Fig 4F). Because the preparation technique excludes the modiolus, only a few ganglion cells could be detected, all apparently showing a variable staining with the neurofilament antibodies.

Desmin and GFAP. No definite immunostaining reaction was observed with our polyclonal and monoclonal antibodies to desmin and GFAP. Questionably specific GFAP-like reactivity was seen at the nerve endings and adjacent nerve fibers of the organ of Corti and in the stroma of the spiral prominence, but only with the polyclonal antibody PGF.

DISCUSSION

In this study we have demonstrated the presence of the IF proteins cytokeratins, vimentin, and neurofilament proteins in the adult human cochlea. With regard to the absence of the remaining IF proteins, however, it should be stressed that negative immunohistochemical staining, without support of direct biochemical analysis, does not definitely prove the absence of the IF protein concerned and therefore is to be interpreted with caution.

In contrast to their absence in the hair cells, cytokeratins were found in all other cells lining the endolymphatic space of the membranous labyrinth. This finding is in accordance with the accepted epithelial origin of these cells and confirms earlier data on cytokeratin expression in the guinea pig and mouse cochleas[6,10,11,14] and the embryonic human inner ear.[8-10] In the organ of Corti immunostaining for cytokeratins occurred in most supporting cells but not in the hair cells. It was most intense in the region of the reticular lamina and in the region of the basilar membrane. In contrast with results obtained in human embryos,[8,9] the tectorial membrane was found to be devoid of immunostaining for cytokeratins as well as for all other IF proteins. The staining in the region of the reticular lamina is in accordance with earlier results in guinea pigs[5,6,10] and human fetuses.[10] As suggested before by Flock et al,[5] Raphael et al[10] have demonstrated that in the guinea pig the presence of cytokeratins in the reticular lamina is restricted to the headplates of the supporting-cell processes, enclosing the apical portions of the sensory cells, which themselves seem to be devoid of cytokeratins or any other IF protein. This is consistent with the absence of immunostaining for cytokeratins and all other IF proteins in both inner and outer hair cells as seen in this study. The absence of IF expression in hair cells is an unusual phenomenon and is not yet understood. It has been postulated that it may reflect the unique mechanical properties of the cells, their polarity, their specialized subcellular structural organization, or the special junctional complexes between hair cells and supporting cells.[10]

In the organ of Corti, the positive immunostaining for cytokeratins at the supporting cells' appositions to the basilar membrane has not been reported earlier.

The "shell"-like distribution of cytokeratins in the supporting cells of the organ of Corti, which "shell" encloses the non–cytokeratin-containing hair cells, suggests a role in determining and maintaining the mechanical structure of the organ. This is in good agreement with the suggested function of cytokeratins, namely maintenance of cell shape and tissue structure by intercellular attachment through des-

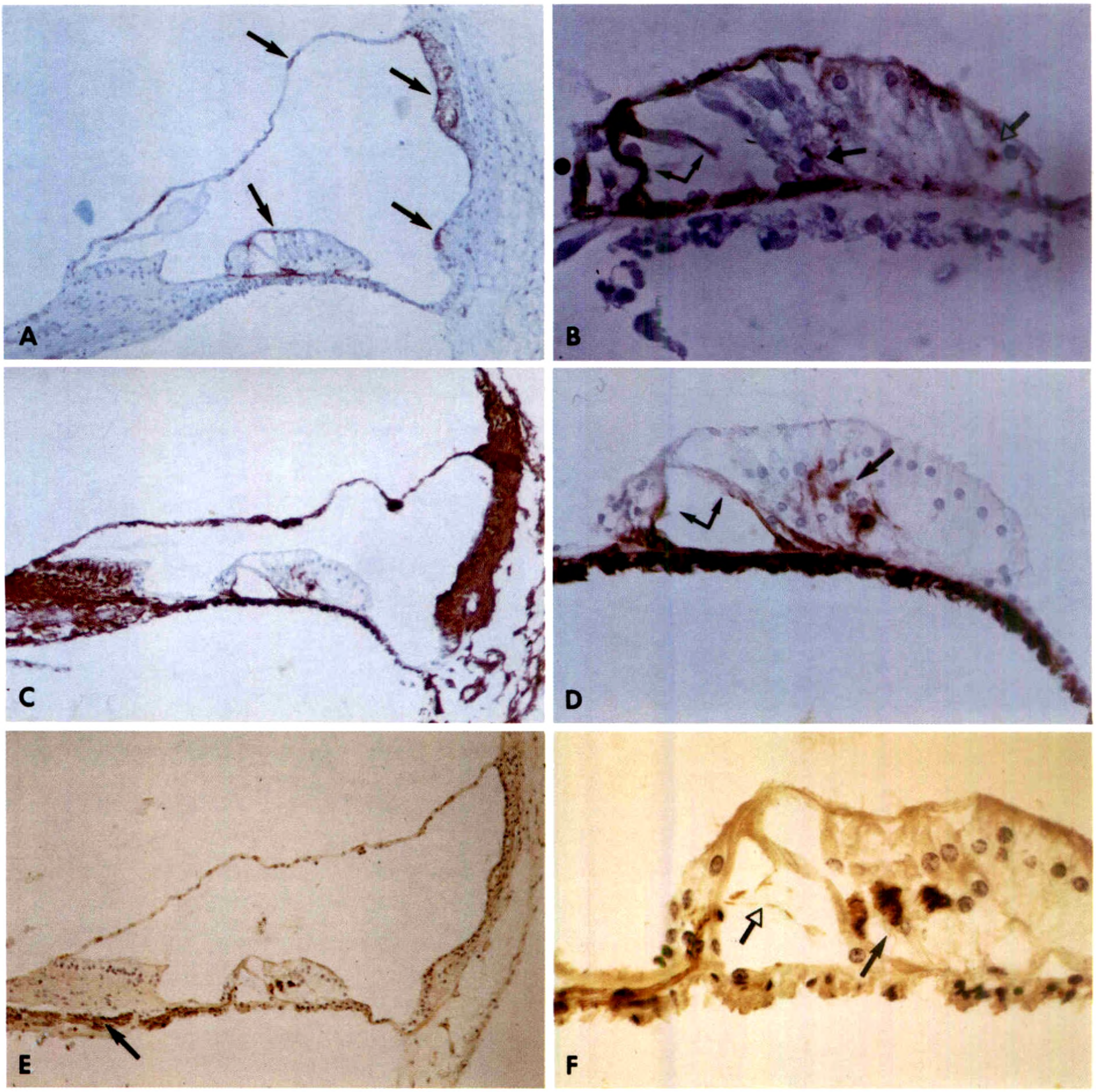

Fig 4. Immunostaining of cochlear duct, with details of organ of Corti. A) Cochlear duct immunostaining with broad-spectrum monoclonal antibody RCK 102 to cytokeratins (original x20). Shows immunostaining of all epithelial cells lining cochlear duct. Shows intense staining of spiral prominence, marginal cells of stria vascularis, Reissner's membrane, and certain regions in organ of Corti (arrows). B) Organ of Corti immunostained with broad-spectrum monoclonal antibody RCK 102 to cytokeratins (original x60). Shows immunostaining of border cells (black dot), inner and outer pillar cells (double arrow), Deiters' cells (dark arrow), and Hensen's cells (light arrow). Shows intense staining at their appositions to basilar membrane and at surface of organ of Corti, to which region these cells contribute. Note absence of immunostaining in hair cells. C) Cochlear duct immunostained with monoclonal antibody RV 202 to vimentin (original x20). Note absence of immunostaining in Claudius' cells, inner sulcus cells, interdental cells, in region of nerve bundles, and in most parts of organ of Corti. D) Detail from C showing organ of Corti (original x50). Immunostaining is limited to inner and outer pillar cells (double arrow) and Deiters' cells (single arrow). Note staining of mesothelial lining of basilar membrane, in contrast to absence of staining in Claudius' cells. E) Cochlear duct immunostained with monoclonal antibody MNF to neurofilament proteins (original x20). Shows immunostaining of neural bundles in osseous spiral lamina (arrow) and of nerve endings at inner and outer hair cells. F) Detail from E showing organ of Corti (original x65). Shows immunostaining of nerve fibers reaching organ of Corti, of nerve endings at inner and outer hair cells (dark arrow), and of tunnel-crossing fibers (light arrow).

mosomes.[22] It has been postulated that the many cytoskeletal and contractile proteins in the reticular lamina are involved in the anchoring mechanism of the stereociliary rootlets and thus could possibly regulate stereociliary stiffness.[23] The presence of cytokeratins in the reticular lamina of the supporting cells, together with their absence in the enclosed apical portions of the hair cells, seems of particular importance since it may be assumed that the resulting difference in stiffness between the sensory and supporting cells plays a substantial role in cochlear micromechanics.

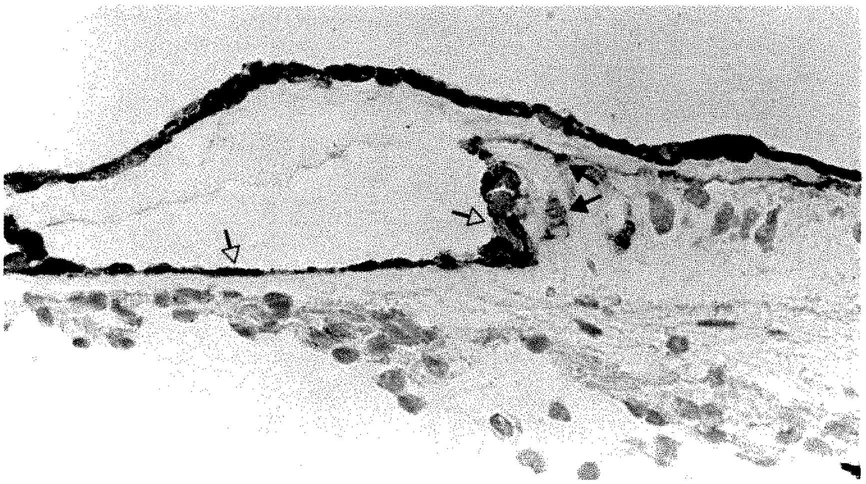

Fig 5. Inner sulcus immunostained with broad-spectrum monoclonal antibody RCK 102 to cytokeratins (original x600). Shows immunostaining of border cells, inner sulcus cells (light arrows), interdental cells (dark arrows), and Reissner's membrane.

Vimentin was found to be present in most supporting structures of the membranous labyrinth. Apart from the region of the neural bundles, the distribution of vimentin appeared to be roughly complementary to the regions of cytokeratin staining, but there were certain cells showing coexpression of vimentin and cytokeratins.

In contrast to initial data obtained in human embryos,[8,9] but in agreement with later results in guinea pigs and mice,[12-14] vimentin was found to be present in the stria vascularis and in the region of the spiral prominence. In the stria vascularis vimentin staining seemed to be limited to the intermediate and basal cells, as has been described by Schrott et al[14] in mice. We could not confirm other guinea pig data[13] reporting additional vimentin staining in the epithelial marginal cells. However, in the region of the spiral prominence, both mesenchymal and epithelial cells showed vimentin staining, and vimentin was also found to be present in the epithelial cells of the outer sulcus. Moreover, staining for vimentin occurred in certain supporting cells of the organ of Corti. This pattern of expression in the organ of Corti differs from earlier conflicting data on vimentin expression in human embryos that either showed staining for vimentin in the outer hair cells and a variable staining in the supporting cells[8,9] or claimed the complete absence of vimentin in all epithelial cells of the cochlear duct, including the supporting cells of the organ of Corti.[10]

Our results on vimentin staining of certain epithelial cells, ie, the region of the spiral prominence and outer sulcus as well as the inner and outer pillar cells and the Deiters' cells in the organ of Corti, demonstrate coexpression of vimentin and cytokeratins since all these epithelial cells were also found to express cytokeratins. However, although resolution was not sufficient to distinguish between the different cell layers of Reissner's membrane, the positive staining for both vimentin and cytokeratins in Reissner's membrane does very likely not reflect coexpression, but is thought to represent vimentin staining of the mesothelial cells and cytokeratin staining of the epithelial cells.

Although determination of coexpression of IFs allows a further characterization of cells and tissues, its meaning is not yet understood. Coexpression of vimentin and cytokeratins has been found in human neuroepithelial tissues but has also been reported in, for example, normal epithelia and mesothelial cells.[13,21] Furthermore, expression of vimentin in addition to another IF protein has been described in many tissues during embryonic development,[4] and this may account for the conflicting earlier data on vimentin expression in the organ of Corti of human embryos.[8,9]

Neurofilament proteins were found in the neural bundles and at the nerve endings at the sensory cells, which themselves showed no immunoreactivity at all. In close agreement with Anniko et al,[8,9] we found only a few nerve fibers ending near the outer hair cells, while the majority were found adjacent to the inner hair cell region. Although neurofilament expression does not allow differentiation between efferent and afferent nerve fibers, one can speculate whether this difference nevertheless in some way does reflect the known difference in innervation between the inner (95% afferent innervation) and outer hair cells (majority of efferent innervation).

We could not confirm earlier results on coexpression of vimentin and neurofilament in the neural bundles of human embryos,[9] since in our material these structures lacked additional staining for vimentin. This difference may be accounted for by the transient expression of vimentin, in addition to another IF protein, in many tissues during embryonic development. Because of limitations set by our tissue-processing technique, our data on neurofilament expression by spiral ganglion cells are too limited to allow conclusions as to the proposed existence of two different populations of spiral ganglion cells based on differences in amount of staining for neurofilament proteins.[9]

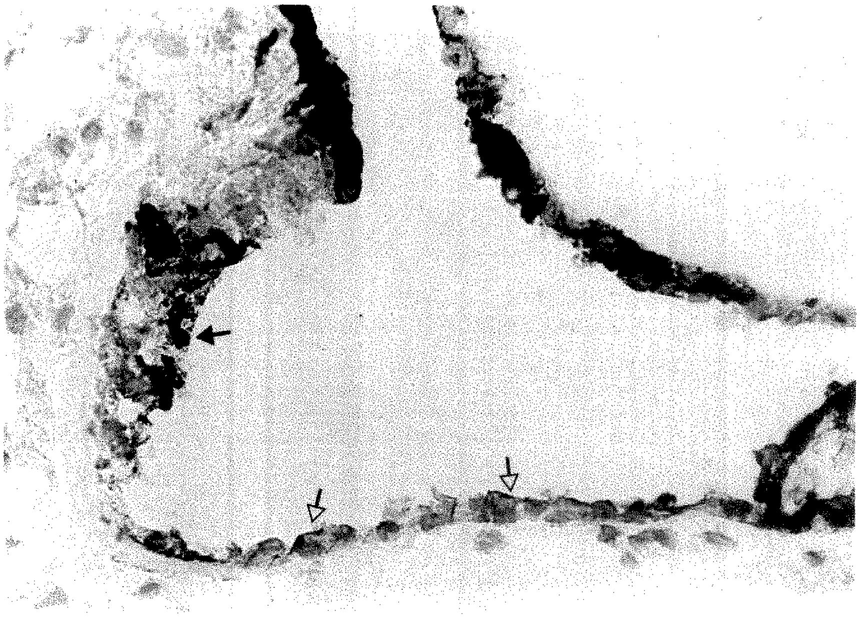

Fig 6. Outer sulcus immunostained with monoclonal antibody RCK 102 to cytokeratins (original x600). Shows immunostaining of spiral prominence, outer sulcus cells (dark arrow), Claudius' cells (light arrows), Hensen's cells, and Reissner's membrane.

No definite immunostaining occurred with our antibodies to GFAP. However, the polyclonal antibody PGF showed reactivity at the nerve endings and adjacent nerve fibers of the organ of Corti without staining the further neural bundles as seen with neurofilament antibodies. In addition, some reactivity occurred in the stroma of the spiral prominence, a region in which neurofilament has never been detected. Unfortunately, these results could not be confirmed by immunostaining with our monoclonal antibody MGF.

The questionably specific GFAP-like reactivity in the spiral prominence seems an interesting finding, since this region is thought to be involved in fluid homeostasis and in the past a possible regulatory function has been suggested on the basis of the finding of somatostatinlike immunoreactivity in this region.[24] Whether our staining results reflect artifacts due to cross-reactivity or reflect the true presence of glia-related cells in the spiral prominence remains uncertain. Further studies with other antibodies and perhaps with a more sensitive (submicroscopic) technique are required to confirm these preliminary results.

In conclusion, the expression pattern of IF proteins in the adult human cochlea as described in this study largely confirms earlier data obtained in several animal species, although some notable differences occurred. Yet, when compared with the results on IF expression in human embryos, there are numerous differences. These differences could be due to the fact that certain tissue types in developing embryos may contain IF proteins different from those present in their adult counterparts.

ACKNOWLEDGMENTS — The authors thank Dr J. C. M. J. de Groot for his valuable remarks and F. Meeuwsen and J. Kuipers-van der Giessen for their excellent technical assistance.

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INTERNATIONAL HEARING AID CONFERENCE: SIGNAL PROCESSING, FITTING, & EFFICACY

The International Hearing Aid Conference: Signal Processing, Fitting, & Efficacy will be held June 21-23, 1991, at The University of Iowa, Iowa City, Iowa. The organizing committee includes Richard S. Tyler, PhD (Signal Processing), Chaslav V. Pavlovic, PhD (Fitting), and Ruth A. Bentler, PhD (Efficacy). Further information may be obtained from any member of the organizing committee at the Department of Speech Pathology and Audiology, The University of Iowa, Iowa City, IA 52242; (319) 335-8726, FAX (319) 335-8851.

Ann Otol Rhinol Laryngol 100:1991

THREE-DIMENSIONAL ANALYSIS OF 61 HUMAN ENDOLYMPHATIC DUCTS AND SACS IN EARS WITH AND WITHOUT MENIERE'S DISEASE

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We used light microscopy and computerized graphic reconstruction techniques to examine the endolymphatic duct and sac in 20 pairs of bones from patients with Meniere's disease and 21 bones from controls. The diameters of the endolymphatic duct and the proximal portion of the vestibular aqueduct were significantly smaller in Meniere's disease ears than in controls. Graphic reconstructions showed the Meniere's sacs to be smaller and to have fewer tubular epithelial structures in the intraosseous portion than in the control ears. The median volume of the sac in the Meniere's disease side was substantially lower than in the contralateral ear. The width of the external aperture of the vestibular aqueduct was significantly smaller in Meniere's disease ears than in controls. These findings indicate that the size not only of the vestibular aqueduct but also of the sac is reduced in Meniere's disease. The results may suggest that the endolymphatic sac is pathologically changed in Meniere's disease and that a reduced resorptive capacity of a small endolymphatic sac could result in endolymphatic hydrops.

KEY WORDS — endolymphatic sac, human, Meniere's disease, three-dimensional reconstructions.

INTRODUCTION

The role of the endolymphatic sac in the development of hydrops and Meniere's disease in humans is still uncertain. Recent evidence indicates that dysfunction of the sac may be a contributing factor but not the sole cause of Meniere's disease.[1]

Studies have shown that the endolymphatic sac may be pathologically changed in Meniere's disease.[2,3] The relationship of this finding to Meniere's disease is inconclusive and contradictory. Several investigators have found hypoplastic vestibular aqueducts in patients with Meniere's disease.[4-6] The functional significance of this finding is not certain; it may indicate that the endolymphatic sac is smaller and has less resorptive capacity in patients with Meniere's disease.

We used three-dimensional (3-D) reconstruction techniques in temporal bones from patients with classic Meniere's disease. We compared the morphologic findings of the endolymphatic duct and sac in Meniere's disease ears, contralateral ears of the same patients, and control specimens. This was done in order to establish if the sac is pathologically changed in Meniere's disease. This investigation is part of a systematic light microscopic and electron microscopic study of the endolymphatic sac in patients with Meniere's disease.

MATERIAL AND METHODS

Sixty-four bones from 32 patients with a clinical diagnosis of Meniere's disease were identified from the House Ear Institute and University of California–Los Angeles collections. Twenty-four of these temporal bones from 12 patients had to be excluded because the diagnosis of Meniere's disease was questionable. The remaining 40 temporal bones were from 20 patients who had fluctuant hearing loss, tinnitus, and episodic vertigo. The bones had endolymphatic hydrops.

The mean age of patients was 73 years (range, 51 to 86 years). The mean duration of the disease was 15 years (range, 1 to 48 years). All bones were removed from 6 to 24 hours after death, placed in formaldehyde, decalcified in Versene, and embedded in celloidin. All temporal bones were cut horizontally at an average thickness of 25 μm and stained with hematoxylin and eosin.

Every 10th section of the 40 experimental bones was used for graphic reconstructions of the duct and sac. The vestibular aqueduct and the epithelium of the endolymphatic duct and sac were magnified 40x with a Bausch and Lomb projector. The outlines of these structures were traced on parchment paper. The diameter of the vestibular aqueduct and sac and the width of the external portion of the vestibular aqueduct were measured. The length of the vestibular aqueduct was determined by multiplying the number of sections from the duct to the external aperture by 25 to account for the distance of 25 μm between sections.

Graphic reconstructions were then fed into an International Business Machines/AT computer using a 3-D reconstruction software program (Jandel Scientific, Corte Madera, Calif). To compensate for

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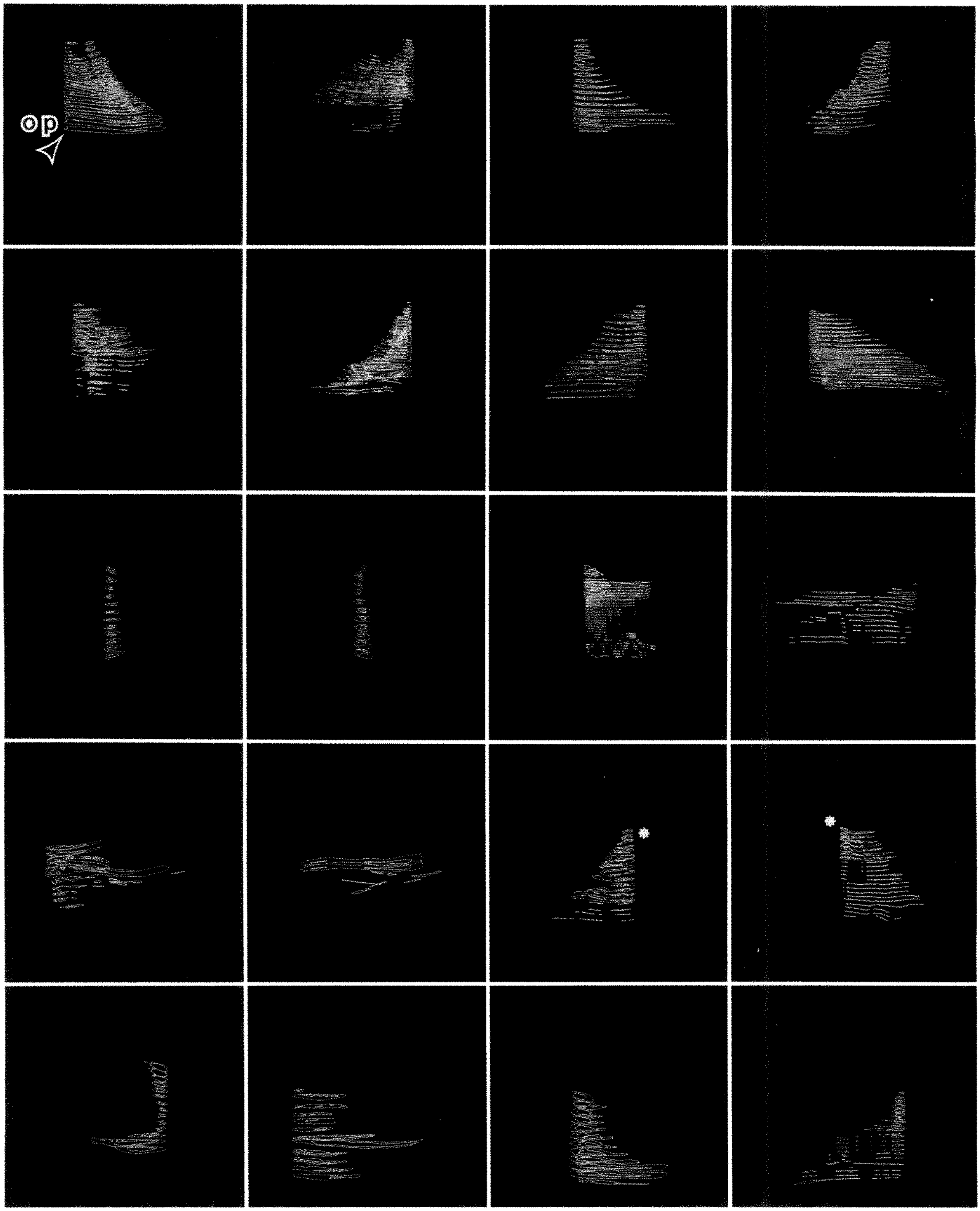

Figure 1A

Fig 1A,B. Computer-based 3-D reconstructions of vestibular aqueduct (blue), endolymphatic duct and sac (green), and area filled with stainable material (red). Columns 1 and 3 — Meniere's disease ears, columns 2 and 4 — contralateral ears. * — bilateral Meniere's disease. A) op — operculum (external aperture of vestibular aqueduct). Note: Computer images result in different magnification factors, making size comparisons of endolymphatic sacs of individual ears invalid.

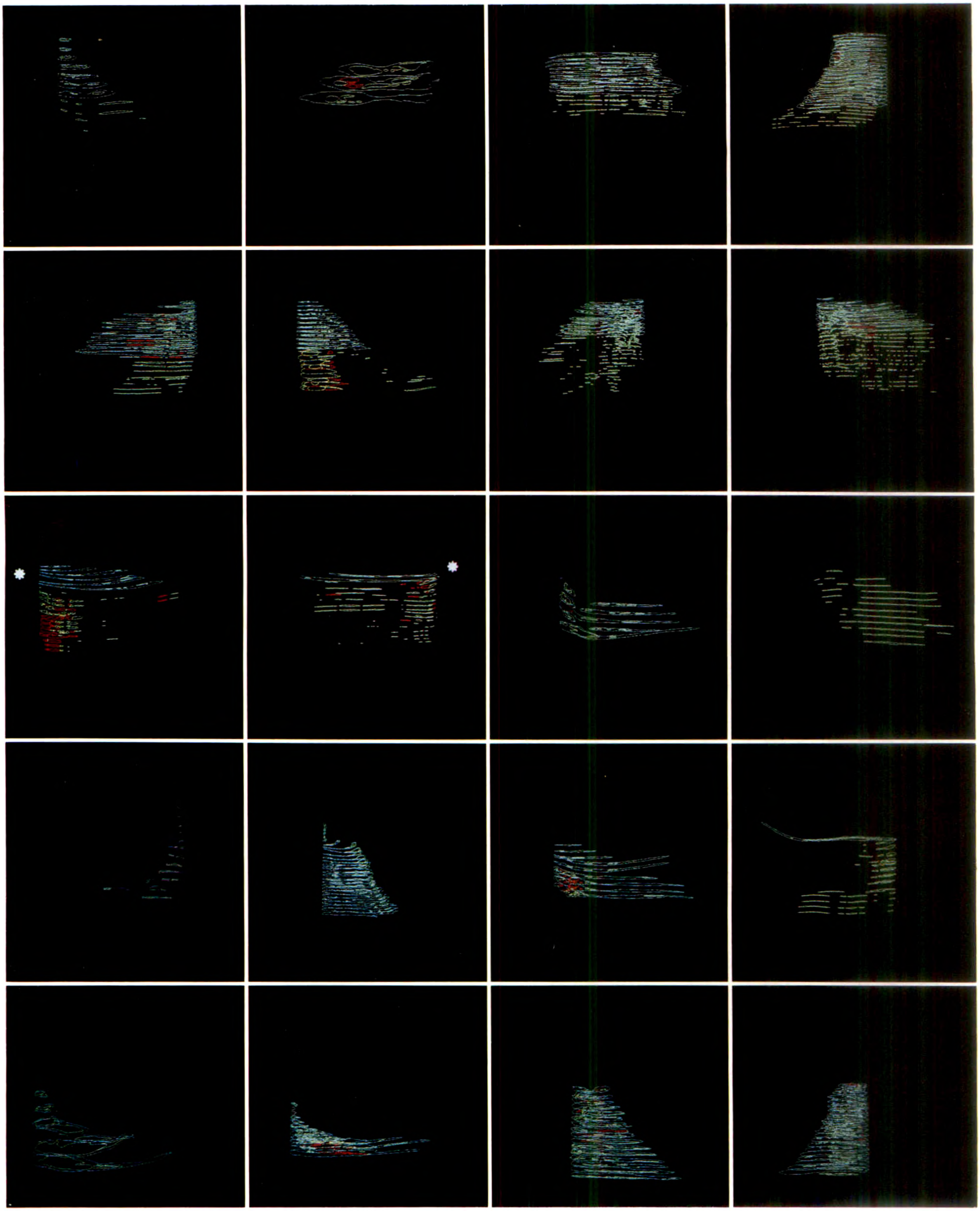

Figure 1B

missing sections, duplicates or triplicates (as necessary) of the section before and/or after the missing section were used.

The volumes of the vestibular aqueduct and sac were assessed by use of the 3-D computer reconstruction software program. The distribution of epithelial tubules of the sac filled with homogeneous substance was mapped with use of the same program. The 3-D reconstructions on the color monitor

DIMENSIONS OF VESTIBULAR AQUEDUCT AND ITS CONTENTS IN MENIERE'S DISEASE, CONTRALATERAL, AND CONTROL EARS

		Ears		
Measure and Structure		*Meniere's Disease (n = 20)*	*Contra-lateral (n = 20)*	*Control (n = 21)*
Diameter of vestibular aqueduct	Mean	0.26 mm	0.27 mm	0.41 mm
	SD	0.08	0.22	0.27
Diameter of endolymphatic duct	Mean	0.12 mm	0.12 mm	0.19 mm
	SD	0.04	0.12	0.12
Width of external aperture of vestibular aqueduct	Mean	4.64 mm	5.08 mm	8.08 mm
	SD	1.76	2.03	6.66
Length of vestibular aqueduct	Mean	2.24 mm	3.03 mm	2.79 mm
	SD	1.08	1.81	0.84
Volume of endolymphatic sac	Median	0.50 μL	0.73 μL	0.78 μL
	SD	1.39	0.62	0.70
Volume of vestibular aqueduct	Median	1.75 μL	3.97 μL	3.14 μL
	SD	2.68	3.00	3.26
Volume of endolymphatic sac filled with homogeneous substance	Mean	0.14 μL	0.10 μL	0.05 μL
	SD	0.25	0.18	0.11

were then photographed with a 35-mm camera. The degree of endolymphatic hydrops was classified as mild, moderate, or severe, and was related to morphologic findings and measurements of the aqueduct, duct, and sac. The experimental temporal bones were classified according to the degree of pneumatization around the vestibular aqueduct: type 1 — large pneumatized cells, type 2 — medium-size cells, and type 3 — no cells around the vestibular aqueduct.[7]

Twenty-one ears from 21 patients with sensorineural hearing loss due to presbycusis were used as controls and matched for patient age and degree of pneumatization. Thus, we studied a total of 61 bones. Nonparametric (Wilcoxon) and Mann-Whitney U tests were used to analyze measurements of structures in paired samples and in index groups, respectively.

RESULTS

Seventeen of the 20 Meniere's temporal bones were of type 3 pneumatization, two were type 2, and one was type 1.

Graphic reconstructions showed striking variations in the gross anatomy of the vestibular aqueduct and endolymphatic sac among both experimental and control specimens. No signs of stenosis or obliteration of the endolymphatic duct and sac were found in any temporal bone. Generally, the sacs in Meniere's disease ears appeared smaller than those in control ears. Often the vestibular aqueducts in Meniere's disease ears and contralateral ears appeared more funnel-shaped (Fig 1). The vestibular aqueduct and sacs in controls appeared more triangular and wider. The intraosseous portion of the Meniere's disease sacs generally contained fewer tubular epithelial structures than did the control ears.

The diameters of the endolymphatic duct and the proximal portion of the vestibular aqueduct (which houses the endolymphatic duct) were found to be significantly narrower in Meniere's disease ears than in control ears (mean values: endolymphatic duct, 0.12 and 0.19 mm [$p < .05$]; and vestibular aqueduct, 0.26 and 0.41 mm [$p < .05$]) (see Table). In the patients with Meniere's disease, the diameters of the endolymphatic duct and vestibular aqueduct in nondiseased ears were not significantly different from those of the diseased ears.

The median volume of the vestibular aqueduct in the Meniere's disease ears was 1.75 μL (range, 0.26 to 10.0 μL), compared to 3.97 μL (range, 0.25 to 9.83 μL) in the contralateral ears and 3.14 μL (range, 0.48 to 6.44 μL) in the control ears. The differences were not statistically significant (Fig 2A).

The median volume of the endolymphatic sac in the Meniere's disease ears was 0.50 μL (range, 0.06 to 1.9 μL), and in contralateral ears, 0.73 μL (range, 0.06 to 2.44 μL) (see Table). The difference was statistically significant with a Wilcoxon nonparametric test ($p < .05$). In control ears, the volume was 0.78 μL (range, 0.11 to 1.24 μL). The difference between Meniere's disease ears and control ears was

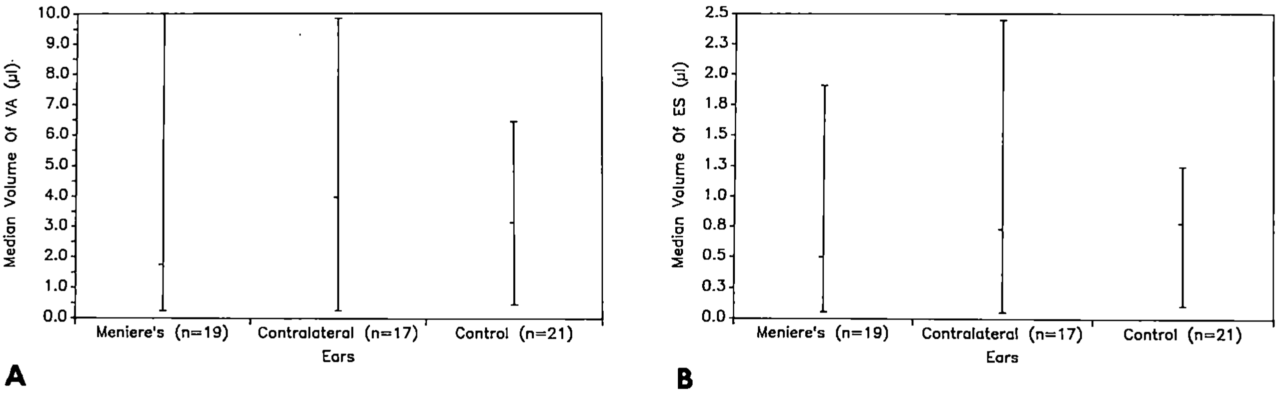

Fig 2. Median and range of volume of A) vestibular aqueduct (VA) and B) endolymphatic sac (ES) in Meniere's disease, contralateral, and control ears.

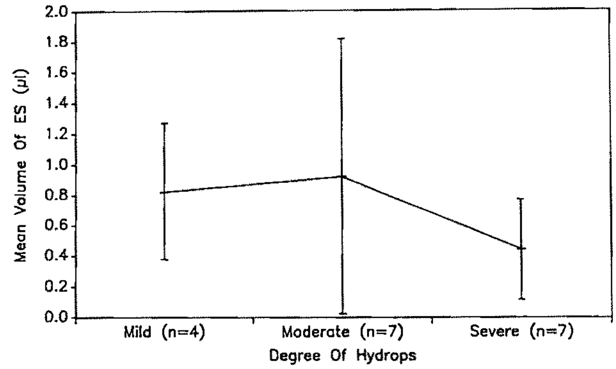

Fig 3. Mean and SD of volume of endolymphatic sac (ES) as function of degree of endolymphatic hydrops.

not statistically significant (Fig 2B).

The mean volume of the endolymphatic sac was smaller in ears with severe endolymphatic hydrops (0.44 µL; SD, 0.32) than in ears with moderate hydrops (0.92 µL; SD, 0.89) or mild hydrops (0.82 µL; SD, 0.44). The differences were not statistically significant (Fig 3).

The mean volume of the endolymphatic sac filled with an eosinophilic stainable substance in Meniere's disease ears was 0.14 µL (SD, 0.25); in contralateral ears, 0.10 µL (SD, 0.18); and in control ears, 0.05 µL (SD, 0.11) (Fig 4A). The differences were not statistically significant. The relative volume of the endolymphatic sac filled with stainable material was 11.99% in Meniere's disease ears, 8.07% in contralateral ears, and 5.14% in controls (Fig 4B). The differences were not statistically significant.

The volume of the endolymphatic sac filled with stainable substance was larger in ears with moderate hydrops than in ears with mild or severe hydrops (0.26 µL, compared to 0.07 and 0.02 µL, respectively) (Fig 5). Differences between the groups with moderate or mild hydrops and between groups with moderate or severe hydrops were statistically significant ($p < .05$). Large amounts of stainable substance were also noted in the contralateral ears of the group with moderate hydrops (0.25 µL).

A linear relationship ($r = .26$) between the volume of the endolymphatic sac and the duration of the disease was not found for our sample (Fig 6A).

The volume of the endolymphatic sac was associated with the width of the external aperture in Meniere's disease ears: small endolymphatic sacs usually had smaller external apertures (Fig 6B). The width of the external aperture of the vestibular aqueduct was significantly smaller in Meniere's disease ears compared to control ears (4.44 and 8.08 mm, respectively [$p < .05$]).

There was no association between the degree of endolymphatic hydrops and the duration of disease (Fig 7).

DISCUSSION

The present investigation indicates that the size of not only the vestibular aqueduct but also the endolymphatic sac is reduced in Meniere's disease. Results also tend to indicate that severe hydrops is associated with a smaller endolymphatic sac. Lesser resorptive capacity in a smaller endolymphatic sac could result in more severe hydrops. Galey et al[8] attributed a reduced resorptive capacity of the sac to fewer small canaliculi in the Meniere's disease ears. They also demonstrated a less rough and more smooth pars canalicularis in the sacs of Meniere's disease ears. Such a clear distinction between rough and smooth canaliculi could not be observed in this material. However, a general decrease in the amount of tubular epithelial structures in the Meniere's disease sacs was noted. This decrease could explain the decrease in the volume of the sac in Meniere's disease.

Earlier histologic and radiographic studies show that the vestibular aqueduct is generally smaller or hypoplastic in Meniere's disease ears compared to normal control ears.[5-7,9,10] The smaller size is expressed by both a lower volume and a smaller width of the external aperture of the vestibular aqueduct. These changes offer explanations to difficulties in the radiographic visualization of this structure in some patients with Meniere's disease.[11-13]

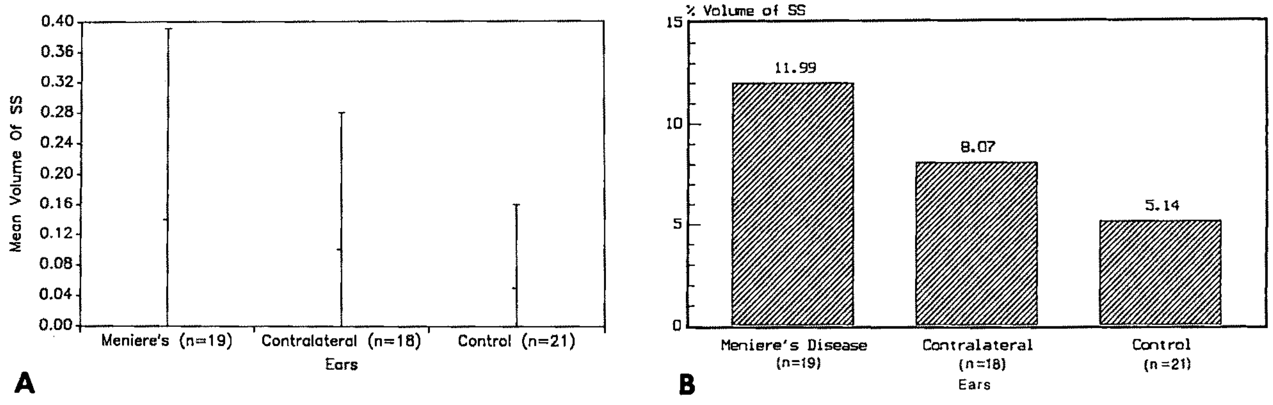

Fig 4. A) Mean and range of volume of endolymphatic sac and B) percent volume of endolymphatic sac filled with stainable substance (SS) in Meniere's disease, contralateral, and control ears.

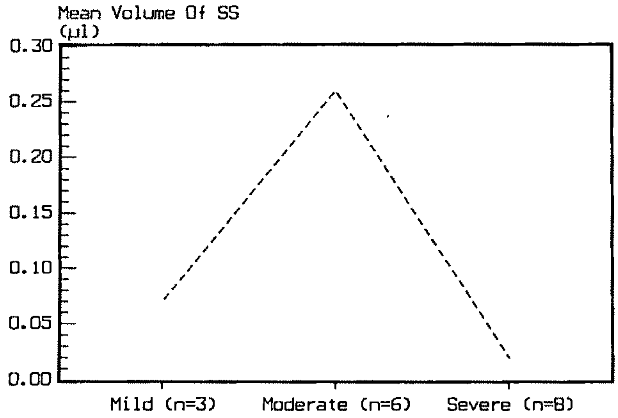

Fig 5. Mean volume of endolymphatic sac filled with stainable substance (SS) as function of degree of hydrops in Meniere's disease ears.

The reason for the reduced size of the vestibular aqueduct in patients with Meniere's disease is not known. Egami et al[4] believed it was due to a congenital hypoplasia of the vestibular aqueduct and endolymphatic sac. Another reason could be atrophic degeneration later in life.

According to Oigaard et al,[14] however, a hypoplastic vestibular aqueduct may be a nonspecific sign of many inner ear disorders. It can be observed in ears with chronic otitis media as well as in individuals with no ear-related diseases but with a low degree of periaqueductal pneumatization.[7]

Variations in fluid pressure, infections, secretory activity, and other conditions affecting inner ear fluid homeostasis could result in anatomic modifications of the endolymphatic sac. This could explain not only the large variations reported by so many authors but also the changes in size and shape of the vestibular aqueduct and endolymphatic sac in diseased temporal bones.

Our finding of no evidence that the sac became smaller or that the degree of hydrops was more severe in ears with a longer duration of the disease seems to indicate that the effects of Meniere's disease on the endolymphatic sac are not linked to the duration of the disease. It is possible, rather, that the size of the endolymphatic sac may be altered early during the course of the disease. If so, this would explain why the reduction in size was not progressive.

The diameters of the endolymphatic duct and vestibular aqueduct (housing the endolymphatic sac) were noted to be significantly smaller in Meniere's disease. Yuen and Schuknecht[15] did not find the diameter of the vestibular aqueduct to be different in Meniere's disease and control ears. Their finding of a smaller duct in Meniere's disease was believed to be a result of the disease rather than the cause of the disease. Since we found that the diameter of the duct was also smaller in contralateral ears, and since these patients did not experience any symptoms in the contralateral ears suggestive of Meniere's disease, this would seem to indicate that it is not a result of the disease. A smaller duct, in fact, could be an important etiologic factor in the development of Meniere's disease.

An interesting finding was more stainable substance in the endolymphatic sac of Meniere's disease ears than in control ears. Sando and Ikeda[6] and Galey et al[8] had similar findings. Sando and Ikeda[6] speculated that the stainable substance could have an unfavorable effect on the resorption of endolymph. Some investigators associated this substance with an increased involvement of immunologic defense mechanisms in the inner ear.[16,17] Still others believe that the substance might be secreted locally[18] or that it could be a protein concentration in the endolymphatic sac resulting from a rapid absorption of water and slower transport of this substance into the surrounding perisaccular connective tissue.[19,20]

In the present study, the accumulation of stainable substance was enhanced in ears with moderate

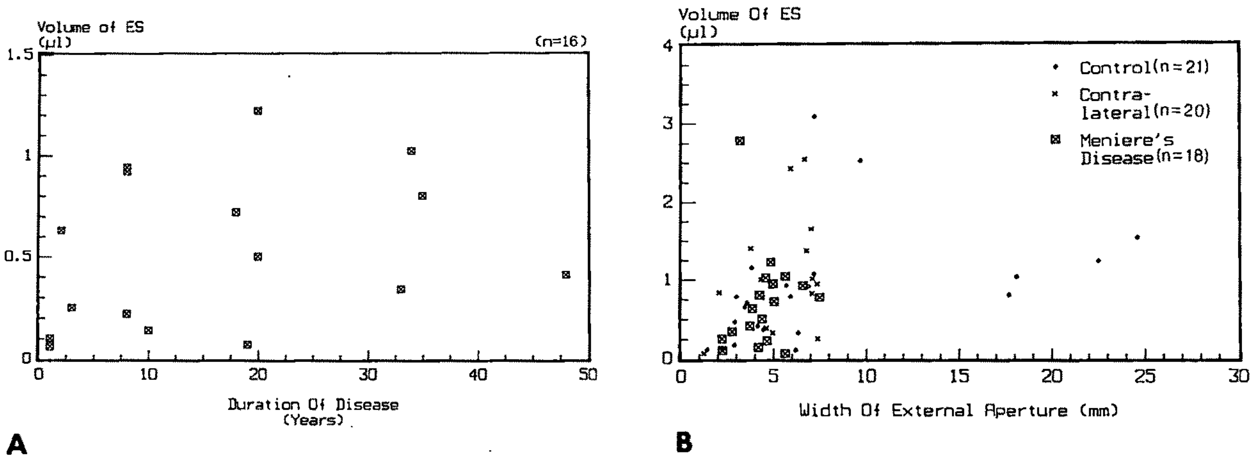

Fig 6. Volume of endolymphatic sac (ES) as function of A) duration of Meniere's disease, and B) width of external aperture of vestibular aqueduct for Meniere's disease, contralateral, and control ears.

hydrops. Why is not known. A review of clinical histories showed that patients whose bones had moderate hydrops suffered frequent vertiginous spells. Perhaps the disease is more active in patients whose bones have moderate hydrops and larger amounts of stainable substance in the endolymphatic sac. Thus, the stainable substance may be related to the formation of endolymphatic hydrops and the cause of Meniere's disease.

Our findings suggest that the endolymphatic sac appears to have a complex function that may be relevant to homeostatic regulation of inner ear fluid volumes. The disturbance in endolymph homeostasis could have resulted from an altered balance in fluid absorption and macromolecular substance secretion or transport in the endolymphatic sac.

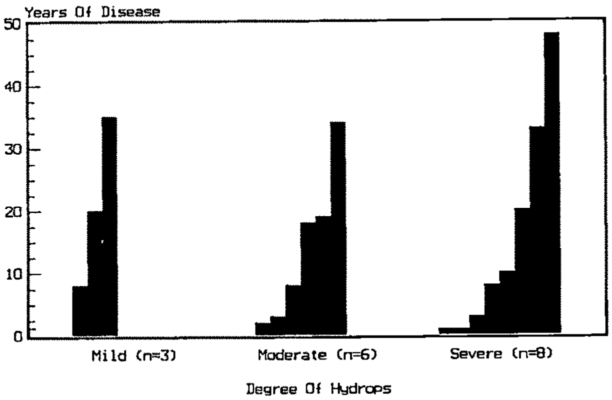

Fig 7. Degree of endolymphatic hydrops as function of duration of Meniere's disease.

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Ann Otol Rhinol Laryngol 100:1991

ADENOIDECTOMY IN OTITIS MEDIA

A REVIEW

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KFAR SABA, ISRAEL

For many years adenoids were thought to affect adversely middle ear (ME) aeration by obstructing the eustachian tube opening, leading to ME infections and effusions. Consequently, the adenoids have often been removed in children suffering from ME diseases; indeed, adenoidectomy is still performed around the globe on millions of children annually. Opinions vary, however, on the usefulness of the operation in various ME diseases. The purpose of this study is to review the available studies concerning the relationship of adenoids to the ME as well as the effect and benefit of adenoidectomy on ME effusions and ME infections.

KEY WORDS — acute otitis media, secretory otitis media, ventilation tube.

BACKGROUND

Acute otitis media (AOM) and secretory otitis media (SOM) are common diseases in children and also occur, although less frequently, in adults. Many infants and children present a significant mass of adenoids in the vicinity of the nasopharyngeal opening of the eustachian tube (ET). These adenoids usually atrophy during adolescence. Experimental obstruction of the ET has been shown to result in middle ear (ME) infection with effusion.[1] A positive correlation has been reported between the bacteria in the nasopharynx and those isolated in the ME.[2,3] It is widely accepted that the ME is normally ventilated through the ET, and it is believed that such ventilation is probably deficient in ME inflammatory syndromes, notably in AOM or SOM, as well as in retractive situations of the drum (atelectasis) and in cholesteatoma.[4] It is also accepted that upper respiratory tract infections in their various forms are more prevalent in winter than in summer and that they may precede AOM and SOM,[5] especially when accompanied by a "running nose."

THEORY

On the basis of the above considerations, the following beliefs have been held for decades.

1. Enlarged adenoids at the opening of the ET will obstruct the tube and result in faulty aeration of the ME, leading in turn to vacuum formation and serum transudation in the ME. It is these events that are often thought to bring about eventually a ME effusion that cannot easily clear itself, ie, SOM. This is the so-called ex vacuo theory.[6]
2. Hearing loss affecting children with SOM can be cured or markedly reduced by adenoidectomy.[7]
3. Upper respiratory tract infections involving the adenoids will infect the ME by extension.[8]

Consequently, over the years adenoidectomy became a routine operation in many centers for the treatment of SOM (and even for other types of conductive hearing loss), to the point at which it ranked among the most common operations worldwide. Fiellau-Nikolajsen et al[9] estimate that 40% of all children in Denmark undergo adenoidectomy; by extrapolation this would put the number of such operations around the globe at several million per year, at a cost of billions of dollars.

However, over the last two decades some doubts have emerged concerning the role of adenoids in ME disease. Many children suffering from AOM or SOM showed no improvement after adenoidectomy.[10-12] Furthermore, adults with SOM, atelectatic ears, or cholesteatoma — conditions in which the ME is significantly underaerated — did not have enlarged adenoids.[13]

Recently, the pendulum has begun to swing back again, with several new studies advocating adenoidectomy in patients with AOM and SOM.[14-16] We therefore felt that the time had come to examine the available information and reevaluate the situation with particular reference to the following hypotheses.

1. The ET tends to be anatomically obstructed, completely or partially, in patients with SOM.
2. In SOM the adenoids are capable of obstructing the ET.
3. Adenoidectomy improves the passage of air through the ET.
4. Adenoidectomy improves immediate and long-term hearing in patients with SOM.
5. Adenoidectomy reduces the incidence of recurrent AOM and SOM.

ANATOMIC OBSTRUCTION OF ET IN SOM PATIENTS

Bluestone et al[17] examined the possible obstruction of the ET in patients with SOM and showed

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that radiopaque material passes freely from the ME to the nasopharynx in such patients. Sadé and Luntz[18] studied serial sections of a large series of temporal bones affected by AOM or SOM and found that the ET was not obstructed. They found also that while the inflammatory reaction in the ET resulted in some narrowing, it occurred mainly in the tympanic part of the tube, which is the widest part of the ET, and diminished progressively along the tube to a minimum in the pharyngeal part, which is closest to the adenoids. Berger et al[19] measured the extent of this inflammatory reaction and found it to be much less in the ET than in the ME itself. These histopathologic studies indicate that the reaction in the ET is most probably secondary to that in the ME.

Two simple studies demonstrated that air could be passed through the ET by politzerization (which produces high unphysiologic endonasal pressures) in over 90% of patients suffering from either SOM or atelectasis.[20,21]

Although the adenoids were thought to hinder mucus clearance in patients with SOM, it was shown[22] that the mucus can be cleared completely simply by the insertion of a ventilation tube (VT) in the tympanic membrane. Thus anatomic, radiographic, and politzerization studies, as well as mucus clearance ability by virtue of a VT, all point to the functional patency of the ET in patients with SOM.

ADENOIDS IN SOM PATIENTS

Gerwat[23] compared the weight of adenoids removed from 39 patients suffering from SOM with that from 29 controls and found no difference between them. Using lateral radiographs of the nasopharynx, Gates et al[24] and Roydhouse[25] found no difference in the size of adenoids between AOM or SOM patients when patients with a good prognosis were compared with those with a bad prognosis. Phillips et al[26] found no difference in the size of adenoids between children with and without ME disease, but found a significant difference in the postnasal space airway between children with SOM and controls. Maw and Parker[16] found the smaller the postnasal space airway (the space between the adenoids and the soft palate), the more helpful the adenoidectomy.

It should be noted that many patients with SOM were found to be devoid of adenoids. Dawes[12] and Mawson and Fagan[27] reported that adenoids were absent in 65% of their patients with SOM, as they had already been adenoidectomized. Similar findings were reported by Kokko.[11] Thus, the second of our hypotheses, like the first, is not supported by the empiric evidence, as there seems to be no difference between SOM patients and controls with regard to either the presence of adenoids or their size.

EFFECT OF ADENOIDECTOMY ON AIR PASSAGE THROUGH ET

Bluestone et al[28] compared ET function before and after adenoidectomy, using a modification of the classic inflation-deflation technique introduced by Ingelstedt and Ortegren,[29] and found that following adenoidectomy, ET function improved in 42% of cases and remained the same or deteriorated in 58%. In a similar study of children with SOM, Honjo[30] found that adenoidectomy did not affect the passive function of the tube, but did improve its "dynamic function." These studies are too contradictory to sustain the hypothesis that adenoidectomy improves the passage of air through the ET.

EFFECTS OF ADENOIDECTOMY ON HEARING LOSS

Immediate Effect. Honjo et al[31] compared the effects of adenoidectomy (as a single procedure) with those of insertion of a VT (also as a single procedure) on immediate hearing improvement in patients with SOM. He concluded that hearing is immediately improved following VT insertion, but not after adenoidectomy. Support for this conclusion comes from Sadé et al,[22] who showed that hearing improves dramatically and almost invariably within 72 hours of VT insertion. Indeed, as clinicians and parents know, after VT insertion an improvement in hearing is already evident a short time after the child awakens from anesthesia. In another study by Sadé[32] VTs were inserted in a number of children, some of whom also underwent adenoidectomy (see below). Comparison of audiograms 2 weeks after the operation revealed that the results in adenoidectomized children were not better than those obtained in children who underwent VT insertion alone.

Indirect testimony to the benefits of VTs, in contrast to those of adenoidectomy, comes from the studies of Maw and Herod[7] and Maw and Parker[16] on a number of patients, some of whom underwent adenoidectomy and some, adenotonsillectomy. Although they tried to evaluate the effect of adenoidectomy on hearing, patients undergoing adenoidectomy also had a VT inserted routinely (unilaterally). Once hearing failed again in these patients — as a result of VT extrusion — the VT was reinserted. Thus, while these authors were ostensibly interested in learning how adenoids affect hearing (see below), their methodology suggests that they relied on the VT rather than on the adenoidectomy for any actual improvement in hearing.

Long-term Effect. Controlled randomized studies of patients with bilateral SOM[7,16] revealed a significant improvement in hearing after 3 years in patients who underwent adenoidectomy as compared with untreated patients. It should again be stressed, however, that these authors found it necessary to insert a VT in the ears of their patients concomitant with the adenoidectomy as well as when hearing deteriorated because of mucus accumulation thereafter.

In a controlled study of patients with SOM who underwent insertion of a VT with or without adenoidectomy, Honjo[30] found that after 6 months of follow-up, hearing was better (15.8-dB gain versus 9.7-dB gain) when adenoidectomy with VT insertion was compared with VT insertion alone. Sadé[32] compared hearing improvement in two groups of patients similar to those in Honjo's study and found that although after 18 months hearing was better in the adenoidectomized group, the difference was not significant.

Other studies[33-35] failed to support these findings. Patients with SOM were divided into four groups: 1) those who underwent adenoidectomy and VT insertion (72 ears), 2) those in whom VT insertion was combined with removal by suction of the ME effusion (35 ears), 3) those with VT insertion but without suction of mucus from the tympanic space (34 ears), and 4) a control group without surgical treatment (78 ears). No significant differences in hearing improvement were detected between the groups after 6 months and again after 12 months of follow-up. These studies were retrospective, but the patients had been allocated to their groups on a random basis — except for one control group that had somewhat milder disease, which was one of the reasons for postponement of the operation.[34] This last group nevertheless demonstrates the need to take into account the essentially benign nature of SOM and its spontaneous favorable long-term natural course. These studies highlight the need to find a means of identifying high-risk and low-risk groups of patients.

In a randomized controlled prospective study Rynnel-Dagöö et al[36] compared the hearing loss in a group of patients who underwent adenoidectomy together with VT insertion with that of a group who underwent VT insertion alone. Two years after operation no differences in hearing (pure tone audiometry) were detected between either of the groups.

Fiellau-Nikolajsen et al[9] conducted a prospective study in which 42 children were randomly allocated to two treatment groups: myringotomy and adenoidectomy (20 children) and myringotomy alone (22 children). Follow-up by impedance audiometry, pure tone audiometry, and otomicroscopy at 1, 2, 3, 21, and 48 months postoperatively revealed no significant differences between the groups.

Honjo et al[31] carried out a controlled study in which 52 children with SOM (76 ears) were divided into five treatment groups: 1) adenoidectomy alone (11 ears), 2) adenoidectomy with VT insertion (30 ears), 3) adenoidectomy with myringotomy, 4) VT insertion for patients with small adenoids, and 5) VT insertion for patients with large adenoids. On the basis of monthly measurements for 6 months, these authors concluded that the least effective treatment was adenoidectomy alone without removal of the ME fluid, while the most effective treatment was insertion of a VT ("when the adenoids were small").

EFFECT OF ADENOIDECTOMY ON INCIDENCE AND RECURRENCE OF AOM AND SOM

In a prospective study by McKee,[37,38] the incidence of AOM in adenoidectomized patients was found to be half as high as in controls during the first postoperative year.

Gates et al[14] carried out a detailed prospective study in which a large population of children with chronic SOM was followed for 2 years with the help of a staff of nurses and family physicians. These children were divided into four treatment groups: 1) myringotomy (107 children), 2) VT insertion (129 children), 3) adenoidectomy and myringotomy (130 children), and 4) adenoidectomy and VT (125 children). The mean time with ME effusion was found to be lowest in patients who underwent adenoidectomy. Some interesting points arise from this study. Most of the patients showed no recurrence, probably because of the short natural course of the disease. Also, those who required surgical retreatment (mainly VT reinsertion) required it only half as often in the adenoidectomized group (36 versus 17). A puzzling finding was that patients with VT insertion were free of effusion for 222 days on the average, while those who underwent adenoidectomy with myringotomy were free of effusion for only 92 days — yet the authors maintain the number of surgical retreatments to be higher in the first group.

Paradise et al[15] conducted a controlled randomized study of 102 children with otitis media who underwent VT insertion with or without adenoidectomy. The number of children free of otitis media was higher in the adenoidectomized than in the nonadenoidectomized group, during both the first year (46% versus 32%) and the second year (54% versus 18%) after the operation. A second controlled but nonrandomized study[15] on 116 children yielded similar results, except that the differences between the two groups were not significant.

In contrast to the above findings, a number of studies have shown no beneficial effect of adenoidectomy on the recurrence of otitis media. In their randomized controlled study Mawson et al[10] found no reduction in AOM in adenoidectomized as compared with nonadenoidectomized patients. Roydhouse[25] followed up patients for several years after their initial assignment to treatment groups in his randomized controlled study. During the first postoperative year, absence of effusion was noted in 82% of children who had undergone adenoidectomy in addition to VT insertion and in 77% of those with VT insertion only; the corresponding findings for the second postoperative year were 85% and 82%. In view of the lack of statistically significant differences between the two groups, Roydhouse concluded that adenoidectomy did not benefit the children and recommended that it should not be employed as the primary form of treatment for SOM. Nevertheless, Roydhouse, like Gates et al,[14] found that fewer adenoidectomized than nonadenoidectomized children needed reinsertion of VTs (53% versus 62%).

Following their prospective study of two randomly chosen groups of patients, one adenoidectomized and the other not, Rynnel-Dagöö et al[36] recorded the incidence of AOM and SOM at the end of both the first and the second years postoperatively. Both groups showed a reduction in incidence of AOM and SOM, but the differences between the two groups were not significant either after 1 year or after 2 years of follow-up.

In a comparison between an adenoidectomized (and myringotomized) group and a group that underwent only VT insertion, Marshak and Ben Neriah[39] found a higher cure rate in the latter group as reflected by the disappearance of ME fluid over a 2-year period. In a similar study Robinson[40] found that the recurrence of otitis media with effusion was not related to adenoidectomy.

DISCUSSION

The history of medicine is replete with episodes in which an apparently logical theoretic notion or hypothesis enjoys wide support by practitioners even when the empiric evidence fails to substantiate it. There are many such cases of refusal to be "confused by facts." For years practitioners pulled out teeth, removed gallbladders and tonsils, and operated on sinuses — all for imaginary focal infections. Appendectomy was performed en masse for so-called chronic appendicitis in cases of vague abdominal discomfort and pain. At other times various treatments have been very popular for a conglomeration of symptoms, as in the case of the famous colitis. (This was admirably described in Axel Munte's *The Story of St Michel* and was also the subject of Bernard Shaw's famous play *The Doctor's Dilemma*.) All these and many other treatments were based on what was considered at the time to be sound logic but could not be backed up by experimental or clinical findings, ie, by what we now consider to be mandatory for scientific proof. We venture to suggest that the widespread use of adenoidectomy for the treatment of SOM is but another example of the acceptance of a "logical truth" unsubstantiated by empiric evidence. The frequent coexistence of enlarged adenoids and SOM has all too often been taken as proof of a direct causal link between these two associated phenomena. This assumption, however, does not appear to be borne out by the facts.

In planning a study aimed at correlating adenoidectomy with improvement of AOM and SOM, one has to take into consideration not only the natural course of the disease but also differences in the course of the disease at various ages and in different populations within each age group. For example, most cases of SOM are mild, and only relatively few are refractory and show a tendency to relapse. In addition, apparent discrepancies between the findings of different studies may be related to the methods of clinical evaluation employed. One might, for example, question the value of otologic data — especially otoscopy — obtained by someone who is not an otologist.

It should also be borne in mind that the detection of statistically significant differences among groups does not by itself necessarily mean that these are in themselves of clinical or practical importance, and for these purposes the magnitude of these differences should be considered.

The proposition that adenoidectomy is a rational treatment that cures SOM and reduces recurrent AOM is obviously simplistic. While none of the available studies is sufficiently comprehensive to take all relevant factors into account, an analysis of the accumulated empiric data nevertheless reveals the following information. First, the ET is not prone to anatomic obstruction in AOM or SOM patients. In those cases in which the ET is narrowed, this narrowing is generally not obstructive, and it occurs mainly in the wide bony part of the ET as a secondary reaction to ME inflammation rather than as its cause.[19] There is also no evidence that adenoids obstruct the ET. Second, the flow of air through the ET, as observed in inflation-deflation tests,[8] does not show a consistent change after adenoidectomy, and the flow of mucus does not depend on the presence or absence of adenoids.[22] Third, there is no difference in the size of adenoids between normal and SOM patients. Moreover, both AOM and SOM can exist in the absence of adenoids. Finally, adenoidectomy by itself does not lead to an immediate improvement of hearing. Hearing loss in patients with AOM or SOM is caused by the presence of an effusion in the ME. There are three ways in which the effusion may disappear.

1. In most cases the disease runs its natural course.

2. Direct surgical evacuation (paracentesis) will restore hearing promptly.

3. Insertion of a VT even without suctioning of the effusion will also promote prompt drainage and will ensure normal hearing and mucus clearance as long as the VT is in place. Indeed, in many of the studies purporting to examine the benefit of adenoidectomy on hearing loss, a VT was inserted at the same time; some authors mention this only incidentally,[16] yet any hearing improvement should

probably be attributed to the VT insertion rather than to the adenoidectomy.

On the other hand, a number of studies show that adenoidectomy may change the natural course of the disease in a certain percentage of cases and reduce the probability of long-term recurrent ME inflammations or reaccumulation of effusion. This reduction, in relation to the entire AOM and SOM population, is not very large, being of about a factor of 2. Most patients with SOM will recover spontaneously within a year; the rest, probably 10% to 20% of the total, will take longer to recover and may require VT insertion at least once.[14,41] From some of the studies[14-16] it would seem that the need for recurrent VT insertion can probably be reduced by half when adenoidectomy is performed. However, this finding is not supported by all studies[9,25,32,36,39] and, if true, applies to only a selected group of patients.

The inescapable conclusion is that adenoidectomy is not indicated as a routine treatment in SOM or in any other type of otitis media. The reason some studies show that adenoidectomy confers benefits on the patient while others do not may have to do with differences in the patient populations studied. Which patients are likely to benefit from adenoidectomy cannot yet be predicted; short-lived cases certainly do not need it, while chronic cases may well continue to recur even after adenoidectomy, as reported by Mawson et al,[10] Kokko,[11] and Dawes[12] — and as any otologist will confirm.

In those cases in which adenoidectomy is followed by reduced recurrence of AOM or SOM, the beneficial effect might possibly be related to the removal of the infective source in the nasopharynx, although this has yet to be demonstrated. Indeed, SOM may be viewed as a subacute otitis media that often follows AOM or any upper respiratory tract inflammation.

In deciding whether or not adenoidectomy is indicated in patients with AOM or SOM, physicians would find it of great help if they could single out those patients likely to benefit from the operation. Maw and Parker[16] claim that patients with a narrow postnasal space benefit from adenoidectomy more than others, for example. Future research should concentrate on the identification of patients likely to benefit, and the operation could then be restricted to this group. That no such study has yet been undertaken can probably be attributed to the low priority given to clinical research. However, the high costs of a suitably designed clinical investigation on the scale required should be weighed against the cost-effectiveness of the adenoidectomies currently performed on millions of children annually. When one takes into account also the operative risks and the doubtful benefits of such treatment, one must seriously question the existing priorities in the medical field.

CONCLUSION

The available studies indicate that most patients with AOM or SOM recover without having their adenoids removed, and that even in extremely chronic and refractory cases the operation often does not benefit the patient. However, when the entire population of such patients is viewed, adenoidectomy, according to some authors, does seem to reduce AOM and SOM *relapse* rate by about a factor of 2, depending probably on the type of population studied. It is not yet known which patients are likely to benefit from adenoidectomy. The central question that is addressed today by most authors is whether in SOM, adenoidectomy or VT insertion should be performed. It seems rather that the question should be whether when VTs are inserted one should or should not also perform an adenoidectomy. Adenoids do not seem to play the major pathogenetic part in AOM or SOM; and when it is desired to clear the ME of effusion in order to restore hearing, a VT is usually placed in the tympanic membrane, even by ardent advocates of adenoidectomy.

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RADIOGRAPHICALLY CONFIRMED COCHLEAR OTOSPONGIOSIS AMONG THE CHINESE

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A high-resolution computed tomography (HRCT) study on 55 patients with surgically confirmed clinical otosclerosis confirms the existence of cochlear otospongiosis among the Chinese. Positive radiographic results of cochlear otospongiosis (13 ears, 12%) were found in patients with mixed-type deafness but in none with conductive hearing loss. Although there is a positive correlation between audiologic and radiographic findings, the HRCT results showed a lower positive rate and less severity than anticipated from the audiologic results. However, compared with the occurrence and extension of radiographic findings in similar studies of white people, it would seem to support our previous contention that the disease is indeed milder in Chinese people. Cochlear otospongiosis with extensive labyrinthine demineralization was found in three young patients with rapidly progressive hearing loss. This is important evidence of the overlooked fact that cochlear otospongiosis may also be one of the causes of sensorineural hearing loss in the Chinese. Thus, a high index of suspicion of the existence of this inner ear disorder is of paramount importance, and in such cases an HRCT study should be performed and sodium fluoride given to prevent further hearing deterioration.

KEY WORDS — cochlear otospongiosis, high-resolution computed tomography.

INTRODUCTION

Otospongiosis, or otosclerosis, is a spongifying disease of the labyrinthine capsule. The site of predilection is the area just in front of the oval window (fissula ante fenestram). If the stapes is involved, conductive hearing loss results. If the membranous labyrinth is involved, whether by extension from the site of predilection or from other cochlear otospongiotic foci, either sensorineural or mixed-type hearing loss results. Despite studies of this condition from many perspectives, including clinical, histopathologic, genetic, enzymatic, and, more recently, autoimmune aspects, the underlying pathogenesis is still unclear.

It has been generally acknowledged, however, that otospongiosis, while frequently found in whites, is rarely see in blacks and Orientals. Our previous clinical, surgical, and histopathologic studies confirmed the existence of otospongiosis in the Chinese.[1] We found that otospongiosis in the Chinese is identical to that in whites in age and sex distribution as well as bilateral involvement, but differs in that the incidence is much lower and no family history was found to exist.[1] Furthermore, the clinical, surgical, and histopathologic findings suggest that otospongiosis in Chinese patients is usually milder than that generally seen in white patients.[1] While a high incidence of mixed-type deafness (90%) would seem to indicate a corresponding high incidence of cochlear otospongiosis, there is a discrepancy between the clinical, surgical, and histopathologic findings and the audiologic results.[1]

The purpose of this paper is to report the findings of high-resolution computed tomography (HRCT) studies on patients with surgically confirmed otosclerosis, in order to provide more definitive data concerning the occurrence of cochlear otospongiosis. An important radiographic finding with regard to sensorineural hearing loss in certain cases is also discussed.

MATERIALS AND METHODS

From November 1988 to October 1989, computed tomography (CT) studies were done on 55 patients (110 ears) with surgically confirmed otosclerosis. In addition, some patients with sensorineural hearing loss were studied, and 3 of these were found to have otospongiosis. One additional case of osteogenesis imperfecta was also studied.

High-resolution CT scans of temporal bones were conducted with a GE 9800 scanner with a 1-mm-thick section. Both axial and coronal plane sections were used.

TABLE 1. TYPE OF HEARING LOSS AMONG PATIENTS WITH SURGICALLY CONFIRMED CLINICAL OTOSCLEROSIS

Type of Hearing Loss	*Men*	*Women*	*Total*
Mixed bilateral	18	20	38
Conductive bilateral	0	3	3
Conductive unilateral	2	3	5
Mixed unilateral	0	2	2
1 mixed, 1 conductive	0	2	2
1 mixed, 1 sensorineural	3	2	5
Total	23	32	55

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TABLE 2. AGE, SEX, TYPE AND DURATION OF HEARING LOSS, AND HIGH-RESOLUTION COMPUTED TOMOGRAPHY FINDINGS OF COCHLEAR DEMINERALIZATION AMONG PATIENTS WITH SURGICALLY CONFIRMED CLINICAL OTOSCLEROSIS

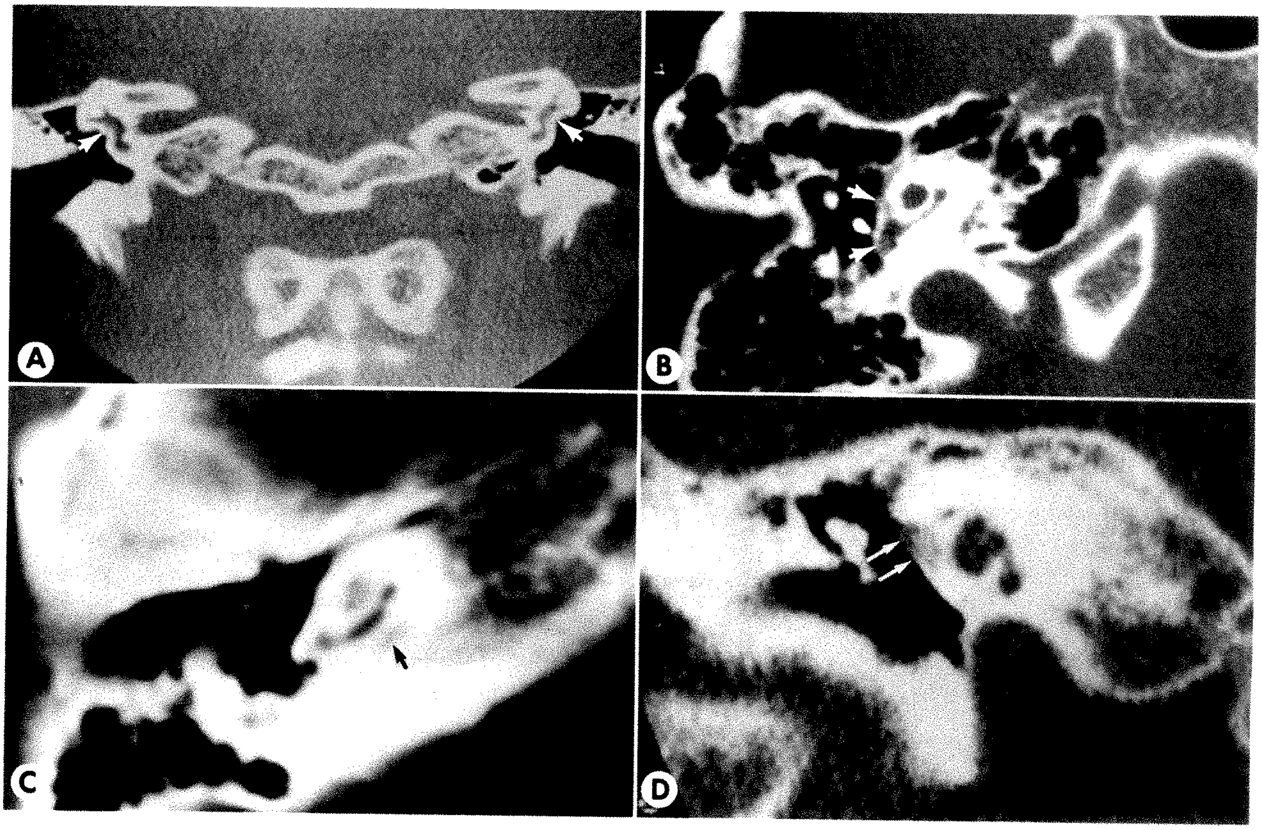
			Hearing Loss		
Pt	*Age*	*Sex*	*Type*	*Duration*	*Radiographic Findings*
1	48	F	B mixed	B 9 y	B promontory demineralization
2	37	F	B mixed	Since childhood	B fenestral obliteration with mature lesion
3	42	M	B mixed	B 9 y with vertigo	Demineralization around R oval window (site of predilection)
4	32	F	B mixed	B 12 y	R promontory wall demineralization with irregular, thickened bone
5	58	M	B mixed	B 1 y	L pericochlear radiolucency
6	54	M	B mixed	B 12 y	Demineralization around R oval window and facial canal (site of predilection)
7	30	M	B mixed	R 16 y L 7 y	B demineralization below oval windows
8	55	M	B mixed	R 7 y L 15 y	B demineralization of oval windows and around facial canals (site of predilection)
9	26	F	R conductive L mixed	6 y 6 y	 L pericochlear radiolucency

B — bilateral.

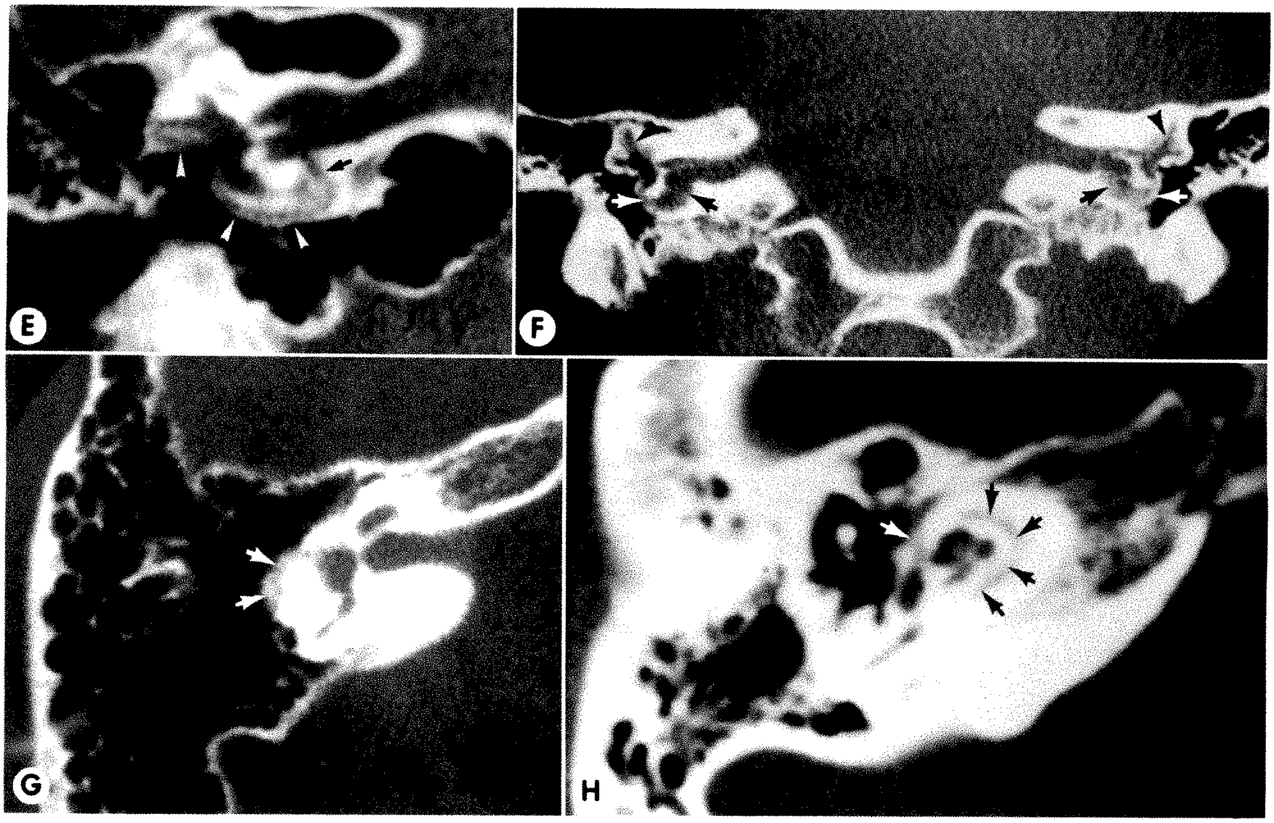
Of the 55 patients, 23 were men and 32 women, and the ages ranged from 30 to 79 for the men and from 20 to 69 for the women. Some were examined radiographically before operation, and some after operation. Thirty-eight of the 55 patients had bilateral mixed-type deafness (Table 1).

RESULTS

Of the 55 patients (110 ears) with surgically confirmed clinical otospongiosis studied, there were positive HRCT findings in 9 (13 ears or 12%). Age and sex of patients, type and duration of hearing loss, and radiographic findings are shown in Table 2.



Computed tomograms. A) (Case 2) Coronal section showing diffusely thickened oval window of both ears (arrows). B) (Case 4) Axial section of right ear (poststapedectomy) showing demineralization over promontory wall with irregular and thickened bone (arrows). C) (Case 5) Axial scan of left ear demonstrating pericochlear radiolucency (arrow). D) (Case 8) Coronal scan of right ear showing demineralization around oval window and facial canal (site of predilection) (arrows). (Continued on next page.)



Figure, continued. E) Coronal section in patient with osteogenesis imperfecta showing severe and extensive demineralization of right labyrinthine capsule (arrowheads). Otospongiotic lucency is so pronounced that there seems to be communication between cochlear capsule and internal auditory canal (arrow). F) (Case 10) Coronal section in 23-year-old man with bilateral total deafness and positive Schwartze's sign showing severe and diffuse otospongiosis of labyrinthine capsules (arrows) involving semicircular canals (arrowheads) of both ears. G) (Case 11) Axial scan in 16-year-old boy with bilateral profound sensorineural hearing loss showing irregular pericochlear demineralization (arrows) of right ear. H) (Case 12) Axial scan in 22-year-old woman with bilateral profound sensorineural hearing loss showing multiple otospongiotic foci with pericochlear zone of radiolucency (arrows).

The audiologic and radiographic findings are well correlated, with positive HRCT results of cochlear otospongiosis only in ears with mixed-type deafness. Even in the only patient with conductive deafness in one ear and mixed-type deafness in the other ear, the findings were positive in the ear with mixed deafness (see Figure, A-D). No ears with conductive-type deafness showed labyrinthine demineralization.

Four additional cases, three with sensorineural hearing loss and one with osteogenesis imperfecta, showed remarkable cochlear demineralization.

One distinctive case was that of a 20-year-old man with a diagnosis of osteogenesis imperfecta who had bilateral conductive deafness, blue sclera, brittle bone, and a positive family history of otospongiosis. This patient underwent a stapedectomy on the right ear. The HRCT revealed severe and diffuse demineralization of the labyrinthine capsules involving the semicircular canals (see Figure, E).

Three otherwise healthy young patients with no other abnormalities but with total deafness or profound sensorineural hearing loss are described in the case reports below.

CASE REPORTS

Case 10. A 23-year-old man complained of progressive hearing loss from the age of 13. The hearing loss in the right ear was more rapid than that in the left ear. At age 16, he completely lost hearing in the right ear, but could still hear with a hearing aid in the left ear. At age 21, in one episode of upper respiratory tract infection, the left ear became totally deaf within 1 day. At presentation at age 23, audiologic test results indicated total deafness in both ears. Otologic examination showed a positive Schwartze's sign in both eardrums. An electronystagmogram with caloric testing revealed canal paresis in both ears. The patient reported that his father had sudden deafness at age 30. High-resolution CT revealed severe, diffuse labyrinthine demineralization involving the semicircular canals and internal auditory canal in both ears (see Figure, F). Currently the patient is being treated on a trial basis with sodium fluoride.

Case 11. A 16-year-old boy had bilateral progressive hearing loss from early childhood. Audiologic results revealed a bilateral symmetric down-sloping profound sensorineural hearing loss with a 90-dB pure tone average but with a speech reception threshold of 60 dB bilaterally and a 76% speech discrimination score. The HRCT scan showed pericochlear irregular demineralization lesions in both ears (see Figure, G). In order to prevent further hearing deterioration, this patient is being treated with sodium fluoride and calcium lactate.

Case 12. A 22-year-old woman had progressive hearing loss for 8 to 9 years in the right ear and sudden hearing loss in the left ear starting 1 year previously. Otologic examination revealed Schwartze's sign in both ears. Audiologic results were 80 dB speech reception threshold in both ears, 28% speech discrimination score in the right ear, and 64% in the left ear, even though the pure tone average was more than 100 dB. An electronystagmogram with caloric testing was normal for both ears. The HRCT scan showed bilateral cochlear demineralization with a pericochlear zone of radiolucency (see Figure, H).

DISCUSSION

This study, using HRCT, confirms the existence of cochlear otospongiosis among the Chinese. In this series of cases of surgically confirmed otosclerosis, approximately 12% (13 of 110 ears) had positive radiographic findings of cochlear otospongiosis, but there were no cases of extensive labyrinthine demineralization.

Reports of other studies with respect to cochlear otosclerosis in the medical literature vary from a positive rate of 18% of surgically proven stapedial otosclerosis by Damsma et al[2] to 100% by Valvassori and Dobben,[3] using cochlear CT densitometry. The studies on whites by de Groot et al[4] reported approximately one-half positive radiographic results in mixed-type deafness. They even found some cases of pure conductive deafness with extensive cochlear demineralization.

This wide variation in results is probably due to 1) a reflection of various stages of otospongiosis, or 2) the difficulty, using radiography, in delineating sclerotic foci from a normal otic capsule or in detecting subtle changes in the labyrinthine capsule. These discrepancies might be accurately defined by the use of cochlear CT densitometry as demonstrated by Valvassori and Dobben[3] and de Groot and Huizing.[5] Besides, some cases reported by Damsma et al[2] showed extensive labyrinthine otospongiosis.

In this study, however, we did not find either the severity of demineralization described by Damsma et al[2] or the positive rate of any other studies on fenestral or cochlear otospongiosis.[5-7] In our previous surgical and histopathologic studies, the high incidence of mixed-type deafness led us to expect a high frequency of cochlear otosclerosis.[1] Contrary to that expectation, this HRCT study, while proving the positive correlation between audiologic and radiographic results, nevertheless substantiates our previous hypothesis that otosclerosis is indeed milder among the Chinese.

In an especially noteworthy group of young patients with progression of sensorineural hearing loss from normal hearing to profound or total deafness within a few years, and usually with a positive Schwartze's sign, radiography revealed much more extensive labyrinthine cochlear otospongiosis (cases 10, 11, and 12). This confirms that otospongiosis has long been overlooked as a cause of sensorineural hearing loss among the Chinese. Even though Valvassori[8] described radiographic changes in the labyrinthine capsule in 60% of his patients with sensorineural hearing loss, to our knowledge there have been no previous reports of cochlear otospongiosis as a cause of inner ear dysfunction in Chinese patients. In cases of this particular type, a regimen of sodium fluoride treatment may prevent further hearing deterioration. A high index of suspicion of the presence of this disease entity is indicated in cases of sensorineural hearing loss, even in Chinese people. Therefore, it is important to emphasize that HRCT scans should be used for early detection of this distinctive and treatable inner ear disorder.

In conclusion, this study confirms the presence of cochlear otospongiosis in patients with surgically confirmed clinical otosclerosis among the Chinese, despite a lower positive rate and less severity than among whites. Furthermore, it also confirms that cochlear otospongiosis is one of the causes of sensorineural hearing loss.

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PATHOPHYSIOLOGY OF *STREPTOCOCCUS PNEUMONIAE* OTITIS MEDIA: KINETICS OF THE MIDDLE EAR BIOCHEMICAL AND CYTOLOGIC HOST RESPONSES

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Streptococcus pneumoniae is an important bacterial pathogen in the pathophysiology of otitis media. To elucidate the inflammatory responses that occur during pneumococcal otitis media, the kinetics of the biochemical and cytologic middle ear responses to heat-killed encapsulated and nonencapsulated pneumococci were studied in the chinchilla model. Inoculation of the middle ear cavity with at least 10^6 *S pneumoniae* cells induced an early, brief vascular response with leakage of small (albumin) followed by larger (α2-macroglobulin) proteins, followed by sustained influx of acute inflammatory cells and lysozyme. The threshold for a sustained lysozyme response was 1,000 times lower for nonencapsulated than for encapsulated pneumococci. These results indicate that nonviable *S pneumoniae* organisms with an intact envelope initiate the middle ear inflammatory response. Therefore, interventions that enhance the clearance of pneumococcal cells from the middle ear may reduce the inflammatory response and prevent chronic middle ear inflammation.

KEY WORDS — bacterial cell wall, inflammation, otitis media, *Streptococcus pneumoniae*.

INTRODUCTION

The mechanism by which bacteria injure middle ear tissues and produce acute otitis media, as well as the role of bacteria in the pathogenesis of chronic otitis media with effusion (OME), has not been carefully investigated. Numerous studies indicate that *Streptococcus pneumoniae* is a principal bacterial pathogen in acute otitis media; this bacterium is cultured from 30% to 40% of acute effusions.[1] In addition, 35% of culture-negative effusions contain pneumococcal capsular polysaccharide antigen; hence, *S pneumoniae* contributes more to the pathogenesis of acute otitis media than is indicated by culture alone.[2]

Since 5% to 10% of all acute otitis media episodes lead to chronic OME, it is possible that retention of subcellular components of *S pneumoniae* in the middle ear after an acute pneumococcal otitis media episode induces and sustains chronic inflammation. Support for this hypothesis is found in studies by Tuomanen and colleagues, who have demonstrated that isolated pneumococcal cell wall invokes inflammation in the rabbit subarachnoid space[3,4] and in rabbit lung.[5] Moreover, we have shown that isolated cell wall induced acute middle ear inflammation in chinchillas.[6]

Previous studies have characterized the continuum of biochemical, cytologic, and histopathologic responses to replicating encapsulated *S pneumoniae* in the middle ear. In chinchillas *S pneumoniae* inoculated into the middle ear leads to massive inflammatory cell infiltration and active middle ear enzymatic responses, such as increases in lysozyme, protease, and protease inhibitors.[7,8] These studies have focused on host responses after the third to seventh postinoculation day, when inflammation is established and purulent effusion is present. Understanding the early kinetics of these biochemical and cellular responses to *S pneumoniae* that lead to middle ear tissue disorders is important to the future design of interventions to prevent chronic OME. These early inflammatory responses were studied in the middle ears of healthy, eustachian tube–obstructed chinchillas. Middle ear fluid (MEF) was aspirated between 2 and 72 hours after inoculation of heat-killed *S pneumoniae* and analyzed cytologically and biochemically.

MATERIALS AND METHODS

A total of 90 healthy 1- to 2-year-old chinchillas weighing 400 to 600 g, with normal middle ears as ascertained by otoscopy and tympanometry, were used for these experiments. Eustachian tube obstruction was performed 1 day before inoculation to prevent the inoculum from flowing out the eustachian tube, as we have described.[9]

Two *S pneumoniae* strains were selected: an encapsulated type 7F (American type 51) strain, which has been used extensively in modeling pneumococcal otitis media in chinchillas,[10] and the non-

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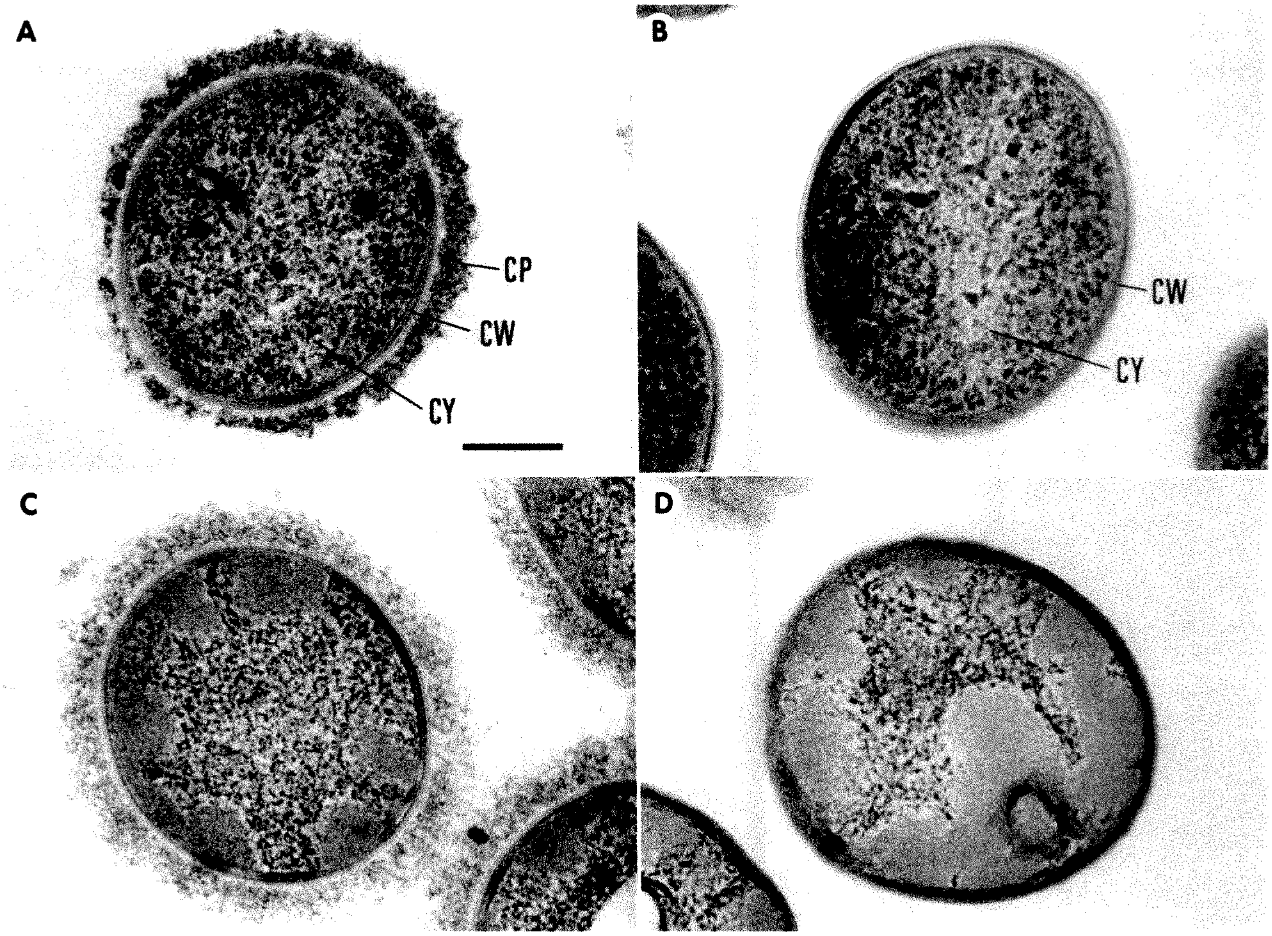

Fig 1. Transmission electron micrographs of A,B) viable and C,D) heat-killed *Streptococcus pneumoniae*. Bar — 0.2 μm, CP — capsular polysaccharide, CW — cell wall, CY — cytoplasm. A,C) Encapsulated type 7F *S pneumoniae*. B,D) Nonencapsulated R6 *S pneumoniae*.

encapsulated pneumococcal strain, R6, which genetically lacks the capsular polysaccharide and derives from a type 2 strain.[3] Pneumococci were incubated 4 to 5 hours at 37°C to log-phase in Todd Hewitt Broth (BBL Microbiology System, Cockeysville, Md) enriched with 35% bovine serum albumin (Sigma, St Louis, Mo). Organisms were rinsed twice in sterile phosphate-buffered saline (PBS, 0.013 mol/L, pH 7.4), heated in a boiling water bath for 10 minutes to kill the cells and inactivate the autolytic enzyme, and rinsed twice in PBS.

Morphologic differences between viable and heat-killed, encapsulated type 7F and nonencapsulated R6 *S pneumoniae* were studied with a transmission electron microscope. Ten-minute immersion in the boiling water bath destroyed the organism's cytoplasm, cytoplasmic membrane, and periplasmic space, but the cell wall of both strains remained intact (Fig 1).

The suspension was adjusted to a concentration of 2 x 10^8 cells per milliliter by use of a Petroff-Hauser counting chamber and diluted to the desired concentration. Killed organisms were cultured on 5% sheep blood agar to confirm absence of viable bacteria and stored at −70°C for no longer than 5 days. A volume of 500 μL of the desired suspension was inoculated directly into the right middle ear cavity through the dorsal bulla; the same volume of sterile PBS was inoculated into the left (control) ear. Sterile PBS was inoculated into both ears of six chinchillas to serve as an external control.

Middle ear effusion was aspirated via the dorsal bulla, as previously described, at intervals of 2, 4, 6, 12, 24, 48, and 72 hours after inoculation.[6] One drop of fluid was inoculated onto 5% sheep blood agar and incubated at 37°C for 24 hours. Only chinchillas whose middle ears remained sterile throughout the study were included in the analysis. Total leukocyte count was determined with a hemocytometer, and leukocyte differential was performed by examining fluid stained with Diff Quick (American Scientific Products, McGaw Park, Ill). Remaining fluid was frozen at −70°C for measurement of lysozyme, albumin, and α2-macroglobulin (α2-MG) at the conclusion of the experiment. Lysozyme concentration was measured with Lysozyme Test Kit Quantiplates (Kallested, Chaska, Minn). Albumin was measured by the single radial immunodiffusion method with use of specific antisera

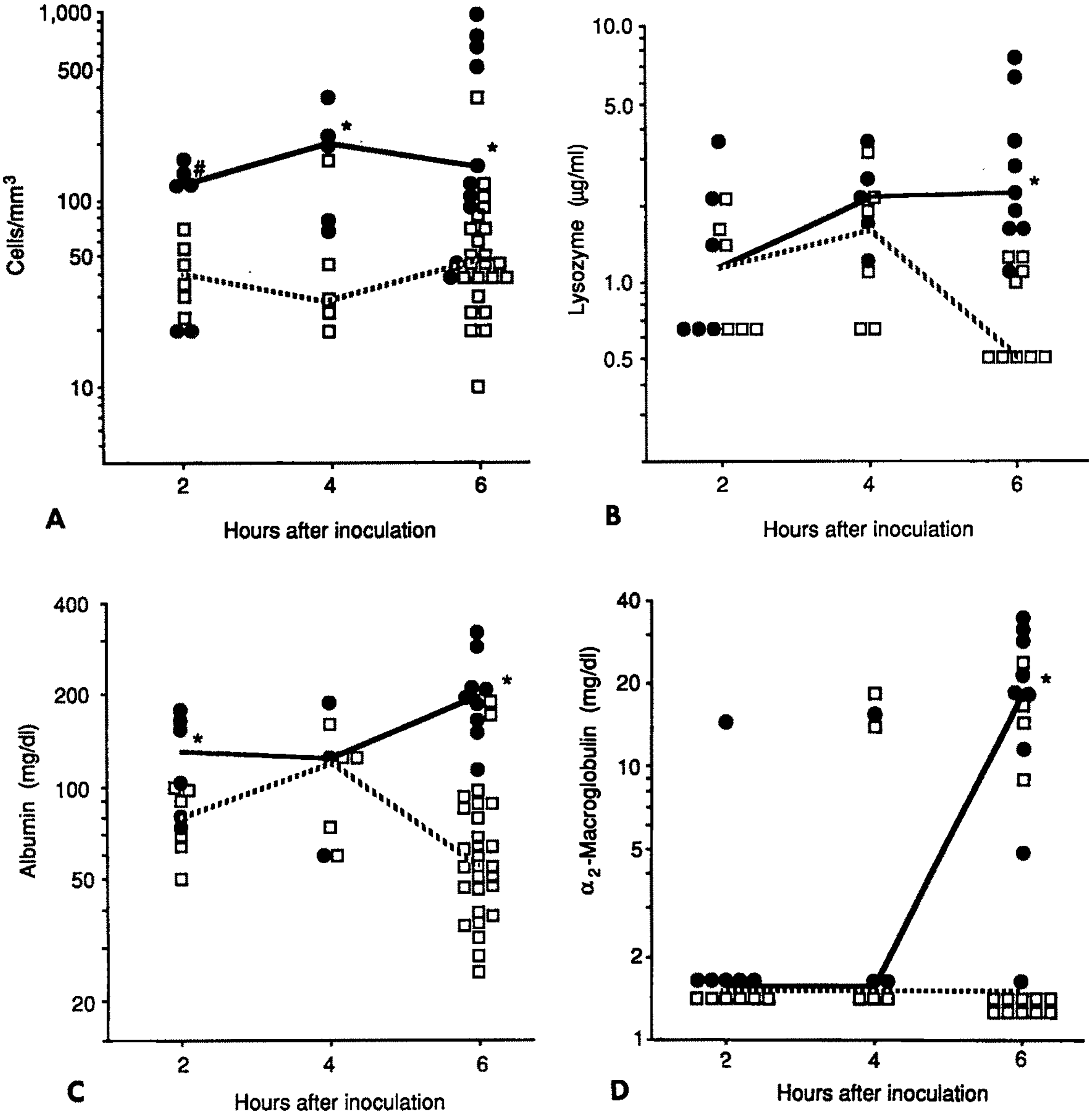

Fig 2. Early inflammatory responses measured in middle ear fluid after inoculation of 10^8 encapsulated pneumococcal cells (circles) or saline (squares). Points — individual values, solid line — median values in experimental ear, broken line — median values in saline control ear, asterisks — $p \leq .05$ difference between groups at time point. A) Inflammatory cells. # — $p = .24$ difference between groups at time point. B) Lysozyme concentration. C) Albumin concentration. D) Alpha 2-macroglobulin concentration.

against purified chinchilla albumin. Purified chinchilla albumin was obtained from whole chinchilla serum.[11] Anti-chinchilla serum albumin was raised in rabbits, and the rabbit serum immunoglobulin fraction was obtained from a diethylaminoethyl cellulose column. Alpha 2-macroglobulin was measured by electroimmunodiffusion with use of specific antisera against purified chinchilla α2-MG.[12,13]

A total of 84 chinchillas were inoculated with the pneumococcal suspensions, and 6 were inoculated bilaterally with sterile PBS. Twenty-one pneumococcal-inoculated animals and one PBS-inoculated animal were excluded from analysis because of intercurrent middle ear infection. Of the 68 chinchillas available for analysis, 40 were inoculated unilaterally with encapsulated pneumococci (12 received 10^8 bacterial cells, 8 received 10^6 cells, 9 received 10^5 cells, and 11 received 10^4 cells), and 23 were inoculated unilaterally with the nonencapsulated strain (8 received 10^8 cells, 7 received 10^6 cells, and 8 received 10^5 cells). All animals had contralateral ear inoculations of sterile PBS.

A volume of 30 to 170 µL (mean, 84 µL) of MEF was aspirated at each sampling time. The number of inflammatory cells in MEF at 48 hours from multiply aspirated ears was not significantly different from the number of cells in MEF from ears aspirated only once at 48 hours (data not shown); therefore, data from single and multiply aspirated ears were combined.

Ears that suffered tympanic membrane perfora-

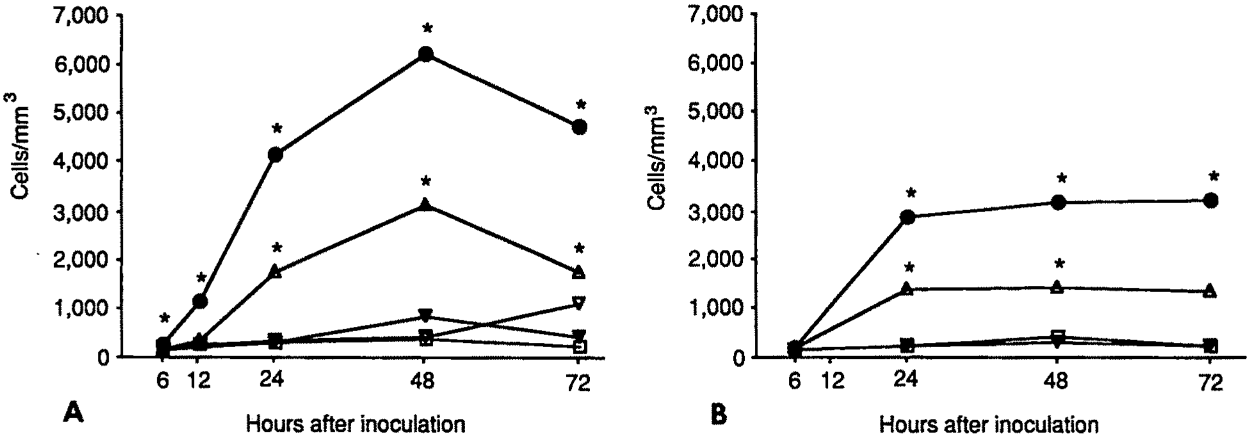

Fig 3. Inflammatory cell concentration in middle ear fluid after inoculation of A) encapsulated type 7F *Streptococcus pneumoniae* and B) nonencapsulated R6 *S pneumoniae*. Median values are shown. Asterisks — significant difference ($p \leq .05$) between experimental and saline control ears, circles — 10^8 cells, empty triangles (point up) — 10^6 cells, filled triangles — 10^5 cells, empty triangles (point down) — 10^4 cells, squares — saline.

tion or bleeding during paracentesis of effusion, and ears with less than 20 μL of fluid aspirated were excluded from analysis; therefore, the number of ears analyzed at each time point varied.

Statistical Analysis. Nonparametric tests, including Kruskal-Wallis for several groups, Wilcoxon-Mann-Whitney for two groups, and Wilcoxon signed rank test for paired comparisons, were used. Because nonparametric tests were used, group values were represented by their median. Tests were two-sided, and no adjustment was made for multiple testing. A p value equal to or less than .05 was considered to be statistically significant. Pearson's test was used to obtain correlation coefficients between two parameters, and a p value equal to or less than .05 was considered to be significant.

RESULTS

Early Inflammatory Responses. Early inflammatory events were measured in MEF 2, 4, and 6 hours after inoculating 10^8 heat-killed encapsulated *S pneumoniae* cells. Pneumococcus-inoculated ears tended to have more inflammatory cells than control ears. Small differences were observed at 2, 4, and 6 hours, but only the differences at 4 and 6 hours were significant (Fig 2A). Two of three ears sampled at all three times showed promptly increasing cell concentrations (190 cells per cubic millimeter at 2 hours to 960 cells per cubic millimeter at 6 hours; and 210 cells per cubic millimeter at 2 hours to 510 cells per cubic millimeter at 6 hours). The MEF albumin concentration was increased significantly in pneumococcus-inoculated ears at 2 hours, and the difference persisted at 6 hours (Fig 2C). All three ears sampled at the three times showed increasing albumin concentration (74 mg/dL at 2 hours to 150 mg/dL at 6 hours; 165 mg/dL at 2 hours to 520 mg/dL at 6 hours; and 80 mg/dL at 2 hours to 210 mg/dL at 6 hours). The MEF lysozyme and α2-MG concentrations were not increased significantly in pneumococcus-inoculated ears until 6 hours (Fig 2B,D). Therefore, increased vascular permeability and inflammatory cell influx were the earliest responses to pneumococcal cells, followed by an increase in lysozyme and vascular leakage of larger proteins.

Effect of Dose and Encapsulation. Encapsulated as well as nonencapsulated *S pneumoniae* cell concentrations equal to or greater than 10^6 induced significant inflammatory cell influx into MEF (Fig 3). Above threshold, dose-dependent inflammatory responses were observed. Inflammatory cell types were quantitated after inoculating 10^8 *S pneumoniae*; polymorphonuclear leukocyte (PMNL) and macrophage influx predominated during the first 6 hours without significant lymphocyte influx during the first 72 hours (Fig 4). The cell differentials did not differ between ears inoculated with encapsulated and nonencapsulated organisms. Therefore, inflammatory cell responses were not influenced by encapsulation.

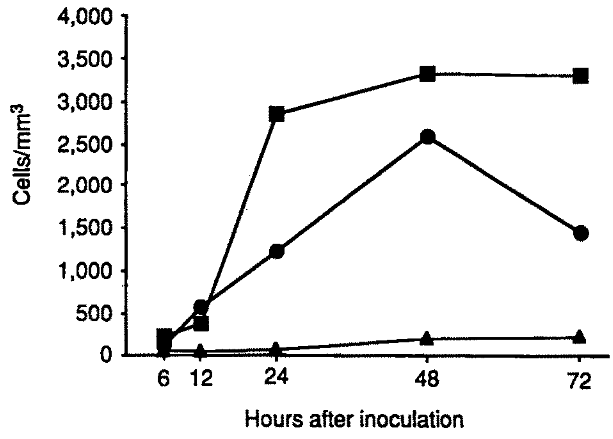

Fig 4. Inflammatory cell types in middle ear fluid after inoculation of 10^8 encapsulated *Streptococcus pneumoniae* cells. Median values are shown. Inflammatory cell types were similar after inoculated nonencapsulated *S pneumoniae* (see text). Squares — polymorphonuclear leukocytes, circles — macrophages, triangles — lymphocytes.

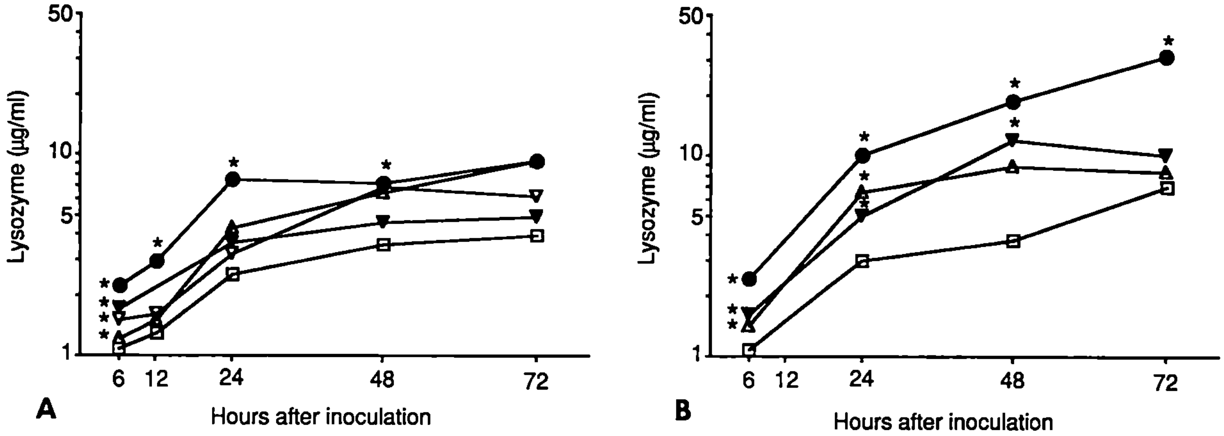

Fig 5. Lysozyme concentration in middle ear fluid after inoculation of A) encapsulated type 7F *Streptococcus pneumoniae* and B) nonencapsulated R6 *S pneumoniae*. Median values are shown. Asterisks — significant difference ($p \leq .05$) between experimental and saline control ears, circles — 10^8 cells, empty triangles (point up) — 10^6 cells, filled triangles — 10^5 cells, empty triangles (point down) — 10^4 cells, squares — saline.

Lysozyme concentration in MEF increased significantly 6 hours after inoculating as few as 10^4 encapsulated cells, but remained significantly elevated only in ears inoculated with the largest number of encapsulated bacteria (10^8 cells) (Fig 5A). In contrast, an early and persistent lysozyme elevation was observed after inoculating as few as 10^5 nonencapsulated pneumococci (Fig 5B). Therefore, the threshold for sustained lysozyme release was 1,000 times lower for the nonencapsulated compared with the encapsulated strain, suggesting that capsular polysaccharide inhibited the host response to pneumococcal cell wall. Lysozyme concentration increased somewhat in control ears because of eustachian tube obstruction.

Correlation coefficients for the relationships between PMNL and lysozyme concentrations in MEF aspirated between 6 and 72 hours after inoculating 10^6 and 10^8 concentrations of *S pneumoniae* were calculated to investigate the source of lysozyme (see Table). The fact that correlation coefficients between 6 and 48 hours were strong for ears inoculated with the encapsulated strain suggests that this lysozyme came predominantly from PMNL. On the other hand, the fact that there was no significant correlation for ears inoculated with the nonencapsulated strain suggests that this lysozyme came predominantly from cells other than PMNLs.

Significant elevation of MEF albumin concentration was observed 6 hours after inoculating as few as 10^4 encapsulated *S pneumoniae* cells, and this response persisted at 72 hours (Fig 6A). A similar response was observed with the lowest dose (10^5) of nonencapsulated bacteria; however, the response was sustained at 72 hours only in the largest inoculum group (Fig 6B).

Encapsulated *S pneumoniae* induced significant α2-MG transudation at 6 hours with bacterial cell doses as low as 10^4; however, this response did not persist beyond 6 hours (Fig 7A). This large protein response was not observed with even the largest dose of the nonencapsulated strain (Fig 7B). Therefore, the vascular response to nonreplicating bacterial cells was early and not sustained, and was dependent on the presence of capsule for transudation of large proteins.

Relationships between PMNL influx and protein transudation were analyzed by determining correlation coefficients between PMNL and serum protein concentrations in ears inoculated with the largest doses of each pneumococcal strain. There were no significant correlations, with only two exceptions, suggesting that the mechanism of PMNL influx differed from that of serum protein transudation.

DISCUSSION

These results provide a new insight into the kinetics of the middle ear inflammatory response to *S pneumoniae*. Increased vascular permeability for small serum proteins was observed within 2 hours after inoculating pneumococcal cells into the middle ear. Inflammatory cell influx followed, as did increasing vascular permeability for larger proteins. Although the vascular response was enhanced by the presence of the organism's capsular polysaccharide, it was sustained, irrespective of encapsulation, only for the small protein, albumin. Both encapsulated and nonencapsulated organisms provided a strong stimulus for inflammatory cell migration into the middle ear. While pneumococcal encapsulation did not affect the cellular response, nonencapsulated organisms appeared to stimulate lysozyme release from more than one source (eg, PMNLs and

POLYMORPHONUCLEAR LEUKOCYTES VERSUS LYSOZYME CORRELATION COEFFICIENTS

Pneumococcus Strain	*Hours After Inoculation* 6	*24*	*48*	*72*
Encapsulated	.883*	.563*	.585*	.205
Nonencapsulated	.335	.397	.124	.309

*Significant correlation ($p < .05$).

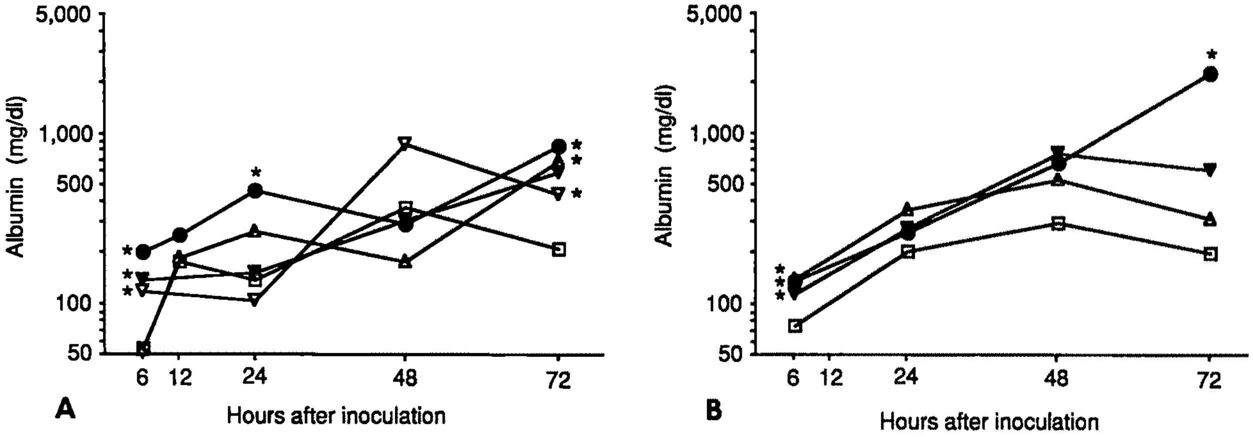

Fig 6. Albumin concentration in middle ear fluid after inoculation of A) encapsulated type 7F *Streptococcus pneumoniae* and B) nonencapsulated R6 *S pneumoniae*. Median values are shown. Asterisks — significant difference ($p \leq .05$) between experimental and saline control ears, circles — 10^8 cells, empty triangles (point up) — 10^6 cells, filled triangles — 10^5 cells, empty triangles (point down) — 10^4 cells, squares — saline.

perhaps middle ear epithelial cells). In this short-term experiment, eustachian tube obstruction caused only mild middle ear inflammation (shown in the control ear) and did not significantly confound the analysis of the bacterial effect on host response.

Understanding the inflammatory response to pneumococcus is important because *S pneumoniae* is frequently the cause of acute otitis media, and because otitis media is a disease continuum; it begins with acute purulent otitis media, progresses to chronic OME in some children, and results in chronic otitis media with intractable tissue sequelae in a few children. An earlier study revealed that 97% of chronic OME patients had histories of prior recurrent acute otitis media.[14] *Streptococcus pneumoniae* is cultured in MEF from 30% to 40% of children with acute otitis media. Moreover, the finding that about one third of culture-negative acute effusions in one study contained pneumococcal capsular polysaccharide antigen indicates that culture underestimates the contribution of pneumococcus to otitis media pathogenesis.[2] Since 5% to 10% of all acute otitis media episodes lead to chronic OME, *S pneumoniae* may contribute to the evolution of middle ear inflammation.

Recent information provides direct evidence that bacteria also contribute to the inflammation of chronic OME. We observed that 35% of the 892 chronic middle ear effusions yielded bacteria on culture, and bacteria (usually gram-positive cocci) were seen by Gram's stain in 17% of 294 sterile chronic effusion samples.[15] Others found MEF bacteria by smear in 80% of OME patients, cultured bacteria in 40% of samples, and noted that mucoid effusion samples contained more nonviable bacteria than serous and leukocytic effusions.[16,17] These results indicated that despite the host's middle ear bactericidal action, clearance of nonviable bacterial cells is impaired in chronic OME. We have hypothesized that pneumococcal cell envelope components retained in the middle ear cavity after an acute otitis media episode induce and sustain chronic middle ear inflammation.

In addition to the present study results, other re-

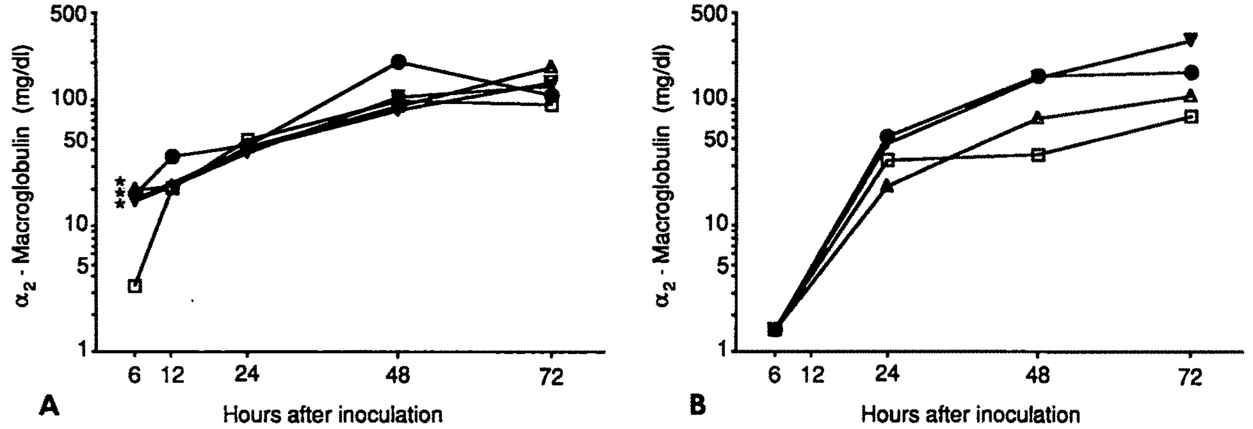

Fig 7. Alpha 2-macroglobulin concentration in middle ear fluid after inoculation of A) encapsulated type 7F *Streptococcus pneumoniae* and B) nonencapsulated R6 *S pneumoniae*. Median values are shown. Asterisks — significant difference ($p \leq .05$) between experimental and saline control ears, circles — 10^8 cells, empty triangles (point up) — 10^6 cells, filled triangles — 10^5 cells, empty triangles (point down) — 10^4 cells, squares — saline.

cent observations support this hypothesis. Ripley-Petzoldt et al[6] measured the histopathologic responses of middle ear mucosa to heat-killed encapsulated and nonencapsulated pneumococci as well as to isolated pneumococcal cell wall. Mucoperiosteal disorders included subepithelial thickening, epithelial metaplasia, granulation formation, and osteogenesis. Tuomanen et al[3,4] reported that heat-killed *S pneumoniae* and cell wall, especially the teichoic acid and peptidoglycan components, that were inoculated into the cistern of rabbits induced meningeal inflammation. Teichoic acid and peptidoglycan each had specific activity high enough to produce an inflammatory meningeal reaction at doses of 10^5 cell equivalents and greater, similar to dose responses with whole bacterial cells in the chinchilla middle ear. Moreover, as in the chinchilla middle ear, capsular polysaccharide did not enhance meningeal inflammation in rabbits, and isolated capsular polysaccharide was relatively noninflammatory in rabbit meninges. However, in a rabbit pneumonia model, the capsule of type 2 and 3 *S pneumoniae* strains played a role in generating pulmonary inflammation.[5] Although the pulmonary inflammatory response to isolated pneumococcal capsular polysaccharide lagged behind the response to isolated cell wall, the magnitude of the response equaled that of the early response to cell wall. Therefore, the contribution of capsular polysaccharide to pneumococcus-induced local inflammation may be organ-specific.

The contribution of lysozyme to middle ear inflammation is not known, although it is a reasonable index of acute inflammation and is known to have antibacterial activity, cleaving the bond between *N*-acetyl muramic acid and *N*-acetyl glucosamine in cell wall peptidoglycan. Therefore, its biologic activity has been associated with host defense.[18] Lysozyme is secreted from both epithelial and inflammatory cells,[19] and it has been suggested that inflammatory cell-derived lysosome may cause middle ear tissue injury.[20] Thus, while lysozyme is a good index of the magnitude of acute middle ear inflammation, further studies are necessary to describe the relationships among lysozyme induced by pneumococcal cells, host defense, and tissue injury.

Concentrations of the serum proteins albumin and α2-MG in nonvascular compartments have been used to assess vascular permeability.[21] The lack of correlation between middle ear inflammatory cell influx and serum protein transudation observed in the present study is consistent with that of previous morphologic studies. For example, electron microscopic study of PMNL migration from capillaries has been characterized by the active involvement of endothelial cells with envelopment of the PMNL by marginal foldlike cytoplasmic processes and of prompt re-formation of the intercellular junction. In contrast, extravascular transudation of plasma proteins was characterized by structural changes in the intercellular junction.[22]

These results suggest that early therapeutic interventions that enhance the clearance of the bacterial cells in the early stage of middle ear inflammation may prevent the development of chronic OME and the resulting pathologic changes characteristic of chronic otitis media.

ACKNOWLEDGMENT — We are grateful to Dawn J. Clawson for performing the electron microscopic studies.

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SIXTH WORLD CONGRESS IN ULTRASOUND

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Ann Otol Rhinol Laryngol 100:1991

PRESSURE RELATIONSHIP BETWEEN PERILYMPH AND ENDOLYMPH ASSOCIATED WITH ENDOLYMPHATIC INFUSION

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The pressure difference between the perilymph and the endolymph following infusion of artificial endolymph into the endolymphatic space was studied in guinea pigs. Both the perilymphatic and the endolymphatic pressures were measured simultaneously with use of two sets of a servo-nulling system. Endolymphatic infusion caused pressure increases in both the endolymphatic and the perilymphatic spaces, but no measurable pressure difference between them. Soon after the endolymphatic infusion, both pressures returned nearly to the initial levels. We conclude that 1) the endolymphatic and the perilymphatic pressures are very closely related, and 2) if a physiologically significant pressure difference exists between endolymph and perilymph in endolymphatic hydrops, it is below the resolving power of the methods used in this study (±0.1 mm Hg).

KEY WORDS — inner ear fluid pressures, servo-nulling system, simultaneous recording.

INTRODUCTION

There are some reports on pressure increase in the endolymphatic space of hydropic animals.[1-3] In these reports, the perilymphatic pressure (Pp) was measured through the round window membrane and then the endolymphatic pressure (Pe) was measured through the basilar membrane. Whether there is a pressure difference between the perilymph and the endolymph is an important issue in relation to the pathophysiology of endolymphatic hydrops.

We previously found that the Pe was dependent on the Pp but that there was no measurable pressure difference between them when the Pp changed.[4]

In this study we simultaneously measured Pe and Pp following endolymphatic infusion to clarify the pressure difference between the endolymph and the perilymph in endolymphatic hydrops.

MATERIALS AND METHODS

Thirty-one healthy guinea pigs weighing about 300 g were used: 26 for the pressure study and 5 for the histologic study. They were anesthetized with an intraperitoneal injection of sodium pentobarbital (25 mg/kg) and immobilized with an intramuscular injection of pancuronium bromide (0.4 mg/kg). Lidocaine hydrochloride (0.5%) was injected into the subcutaneous tissue where the operative incision was to be made. A tracheostomy was performed and artificial respiration was provided. The cochlea was reached via the superolateral approach. The body of the animal was wrapped in a heating blanket to maintain body temperature. Supplemental sodium pentobarbital (20 to 25 mg/kg) was administered intraperitoneally before the pressure study.

The perilymphatic space was accessed through a small hole of about 50 μm in the bony wall of the scala tympani of the basal turn. Access to the scala media was gained by thinning the bony cochlear wall over the stria vascularis of the basal turn and making a small fenestration (about 50 μm in diameter). To measure the Pe and to infuse artificial endolymph, two fenestrations were made in the bony wall of the scala media (Fig 1). The distance between the two fenestrations in the scala media was about 1.5 mm.

The pressures of the inner ear fluids were measured by use of two sets of a servo-nulling system (Micropressure System Model 900, WPI Inc, New Haven, Conn). The advantages of using two sets of this system were discussed in another paper.[4] They were precisely calibrated to show the same value for the same applied pressure. The capillary micropipettes that we used to measure the pressure had been beveled and the tip diameters were about 5 μm. They were filled with a 2 mol/L potassium chloride solution. The pipette insertion into the endolymphatic space was confirmed by simultaneous recording of the endolymphatic DC potential (EP) over 60 mV.

To infuse artificial endolymph, a specially constructed device was used (Fig 2). The micropipette (15 to 25 μm in tip diameter) was connected to a very thin heat-pulled polyethylene tube with a volume scale and filled with artificial endolymph (Table 1[5]), of which the composition was described previously by Marcus et al.[5] A microsyringe connected to the polyethylene tube was used to apply pressure for infusion. The location of the tip of the micropipette was confirmed by recording an EP over 60 mV with an electrometer (Dual Electrome-

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From the Department of Otolaryngology, Kochi Medical School, Kochi, Japan. Supported by grants from the Japanese Ministry of Education (61570825, 63771323) and from the Japanese Ministry of Welfare (Research Program for the Vestibular Disorders).

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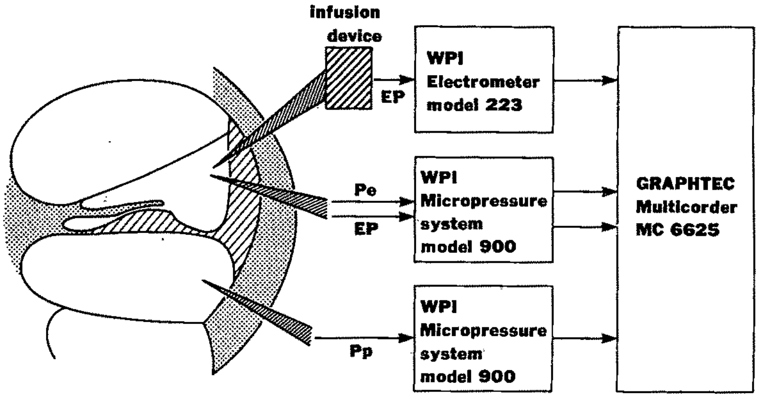
Infusion device
EP
WPI Electrometer model 223
Pe
EP
WPI Micropressure system model 900
Pp
WPI Micropressure system model 900
GRAPHTEC Multicorder MC 6625

Fig 1. Block diagram of experiment. Both perilymphatic pressure (Pp) and endolymphatic pressure (Pe) were measured simultaneously and artificial endolymph was infused into scala media. EP — endolymphatic DC potential.

ter Model FD223, WPI Inc).

The three sites of pipette insertion, two for pressure measurement and one for endolymphatic infusion, were sealed with dental cement (Unident SMFP, Sankin Inc, Osaka, Japan) to prevent leakage. According to the data of Fernandez,[6] the volume of the scala media of a guinea pig is about 2 μL. We infused 2.0 μL of artificial endolymph into the scala media to make a significant volume increase in the scala media. The time required for the infusion was 0.5 to 4 minutes. After the infusion, no backflow of endolymph into the infusion device was seen.

Cochlear histology studies were performed on five animals that were painlessly killed immediately after a 2-μL infusion of artificial endolymph. These animals were used for the histologic studies only. Their temporal bones were removed after vascular perfusion with fixative (10% neutral formalin) and immersed in the same fixative. They were decalcified and paraffin blocks were made after immersion in 1% celloidin solution for 4 days.

RESULTS

Simultaneous pressure recordings of Pp and Pe and endolymphatic infusion were successful in 12 of 26 guinea pigs. In the other 14 guinea pigs, one or both pressures could not be measured because of pipette plugging or low EP recording in the scala media.

Since there is no difference between Pp and Pe in normal guinea pigs[1,2,4] and the absolute pressure value of the inner ear fluid varies from animal to animal, and also in the same animal by postural changes, only pressure changes were studied and absolute pressure was not measured.

Figure 3 shows the changes of Pe and Pp associated with endolymphatic infusion. During the infusion of artificial endolymph, both Pe and Pp showed simultaneous dynamic changes and the increases of Pe and Pp were almost the same. Soon after infusion, both Pe and Pp returned to nearly the same levels as before infusion.

The differences between Pe and Pp after 0.5-, 1.0-, and 2.0-μL infusions and EP values before infusion in 12 guinea pigs are shown in Table 2. These measurements were made on the same trace. There are no statistically significant differences between Pe and Pp at each point. The resolving power of the methods used in this study is ±0.1 mm Hg when the pressure-measuring system including the micropipettes is adequately adjusted. In 2 animals (Nos. 6 and 10) the EP values were relatively low, but the results of the pressure study do not indicate that animals with a relatively low EP show a smaller pressure difference compared to the animals with normal EP values. There were some pressure gradients in some animals. However, both positive and negative gradients existed, so these data do not indicate that Pe is higher than Pp. These gradients in data might be caused by the slight bending of pipettes or by some other unknown artifact.

In no animal was there fluid leakage from the round window or backflow into the infusion pipette after infusion.

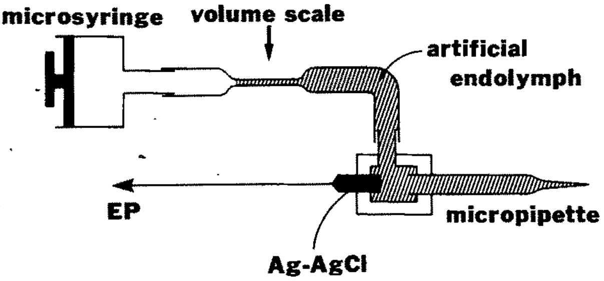

Fig 2. Device for infusion of artificial endolymph. EP — endolymphatic DC potential.

TABLE 1. COMPOSITION OF ARTIFICIAL ENDOLYMPH

Agent	*Concentration (mmol/L)*
Potassium chloride	126.0
Sodium chloride	1.0
Potassium bicarbonate	25.0
Magnesium chloride	0.025
Calcium chloride	0.025
Dipotassium phosphate	1.8
Potassium phosphate	1.4
Mannitol	25.0

Information from Marcus et al.[5]

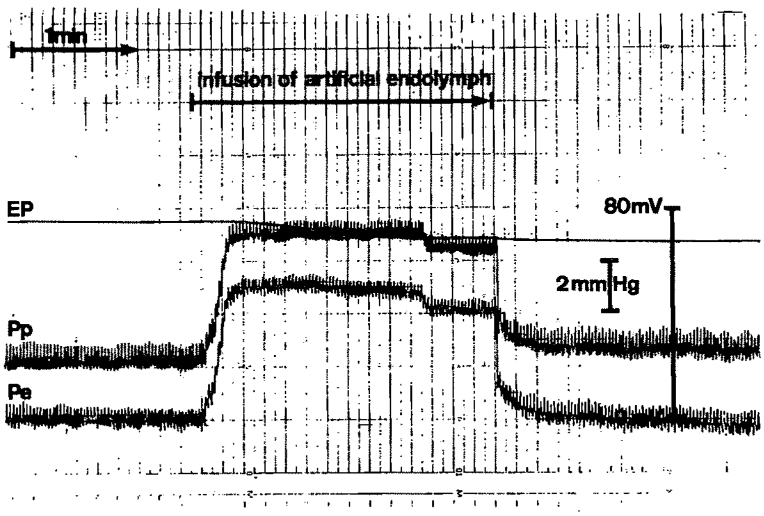

Fig 3. Effects of artificial endolymph infusion on perilymphatic pressure (Pp), endolymphatic pressure (Pe), and endolymphatic DC potential (EP).

The peak Pe during infusion and the difference in Pe between before and 1 minute after infusion is shown in Table 3. Because Pp showed almost identical changes as Pe, only Pe values are shown. Soon after the infusion, the Pe (and also the Pp) decreased quickly (Fig 3). The peak pressure varied from animal to animal because of the variation of infusion speed, which resulted from the variation of the tip diameters of the infusion pipettes (15 to 25 μm), although the pressure applied on the microsyringe of the infusion device was not varied. A slight change in the tip diameter resulted in a relatively great change of resistance for the infusion.

Histologic features in every specimen after the 2-μL infusion were mild distention of Reissner's membrane (Fig 4A) and the saccule (Fig 4B). There was no evidence of any rupture of the membranous labyrinth. There was not any evident variation across animals with respect to the degree of hydrops.

The EP value decreased as a result of the endolymphatic infusion, but nearly recovered shortly after infusion (Fig 5).

TABLE 2. PRESSURE DIFFERENCE BETWEEN ENDOLYMPH AND PERILYMPH ASSOCIATED WITH ENDOLYMPHATIC INFUSION

	*Infusion Volume (μL)**			*Endolymphatic DC Potential*
Animal	*0.5*	*1.0*	*2.0*	*(mV)*
1	0.0	0.2	−0.2	80
2	0.0	−0.2	−0.2	85
3	0.0	−0.3	0.0	78
4	0.0	0.0	0.0	81
5	0.0	0.0	0.0	81
6	0.0	0.0	0.0	62
7	0.1	0.2	0.0	80
8	0.0	0.0	0.2	86
9	0.0	0.0	0.2	82
10	0.1	0.1	0.2	70
11	0.0	0.0	0.0	82
12	0.0	0.0	0.0	86
Mean	0.017	0.000	0.017	
SD	0.037	0.135	0.128	

*Values are endolymph pressure minus perilymph pressure in mm Hg.

DISCUSSION

The endolymphatic infusion in this study caused a very acute increase in the volume of the endolymphatic space, and this was a model for the formation of endolymphatic hydrops in a very short period of time. Simultaneous pressure recordings of perilymph and endolymph showed the pressure relationship of the perilymph and the endolymph associated with endolymphatic volume increase. During and after the endolymphatic infusion, Pe and Pp showed simultaneous changes and there was no measurable pressure difference between Pe and Pp. This may mean that there is no measurable pressure difference between Pe and Pp not only after the formation of endolymphatic hydrops but also during it.

In the previous report, we showed that the pressure change in perilymph was transmitted to the endolymph directly and there was no pressure difference between Pp and Pe associated with Pp changes.[4] We found in this study that there is a direct pressure transmission in the opposite direction, from endolymph to perilymph.

TABLE 3. PEAK PRESSURE OF ENDOLYMPH DURING INFUSION AND PRESSURE DIFFERENCE OF ENDOLYMPH BEFORE AND AFTER INFUSION

Animal	*Peak (mm Hg)*	*Difference (mm Hg)*
1	>16.0	0.4
2	>16.0	0.7
3	5.2	−0.2
4	2.0	0.4
5	1.8	0.6
6	1.1	0.0
7	1.5	0.3
8	4.1	0.2
9	3.2	0.3
10	12.4	1.2
11	11.8	0.6
12	10.8	0.5

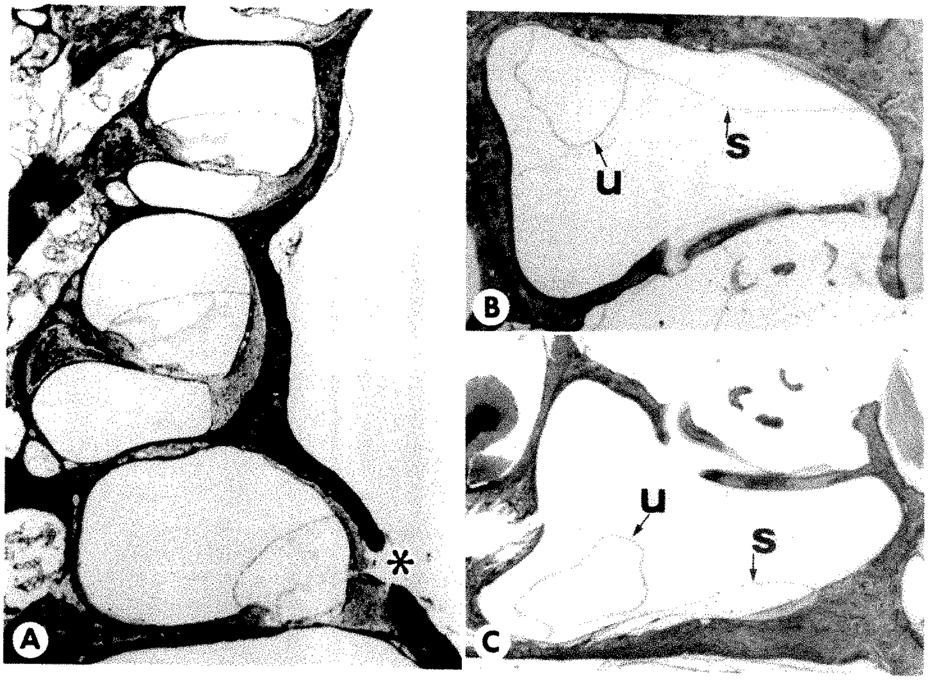

Fig 4. Histology after 2-μL infusion of artificial endolymph. A) Cochlea. Shows mildly distended Reissner's membrane. Asterisk — pipette insertion site into scala media. B) Vestibule of infused side. Shows mildly distended saccule (s). u — utricle. C) Vestibule of normal side. s — saccule, u — utricle.

After the endolymphatic infusion, both Pe and Pp decreased quickly. The volume increase in the cochlea may be compensated for by the shift of the perilymph into the cerebrospinal fluid space via the cochlear aqueduct and the internal acoustic meatus. The cochlear aqueducts in humans are not as patent as those of guinea pigs, so it may take a long time for the increased pressure in the inner ear fluids caused by an acute volume increase in the cochlea to return to the normal value.

A mildly distended Reissner's membrane and a distended saccule were evident in histologic specimens after a 2-μL endolymphatic infusion. This finding verified that the endolymphatic infusion could be a model of very acute endolymphatic hydrops. Electrode insertion provides a potential source of damage to the boundary between the endolymph and perilymph, but the histologic results suggest that the possibility is very small. The lack of evidence of a difference between Pe and Pp even during the rapid infusion of the artificial endolymph may suggest that excess pressure in the endolymphatic space is not a causative factor for the distention of Reissner's membrane in endolymphatic hydrops.

Tasaki et al[7] reported that an injection of isotonic potassium chloride solution with a volume of about 0.015 μL into the scala media caused an increase in the EP. The decrease of EP following endolymphatic infusion in our study might be the result of the temporary anoxia of the stria vascularis caused by the pressure increase in the cochlea, because the infused volume into the scala media in our experiment was 2.0 μL, which was more than 100 times that of Tasaki et al. The tendency for the EP value to recover after the endolymphatic infusion may suggest that this manipulation did not cause irreversible change in the EP production system and that the electrical state of the endolymphatic space was not severely damaged.

We speculate that the symptoms of endolymphatic hydrops, such as hearing loss and vertigo, may not be the result of "endolymphatic hypertension." Volume increase of the endolymph and changes related to this volume increase may be important factors in the genesis of the symptoms of hydrops.

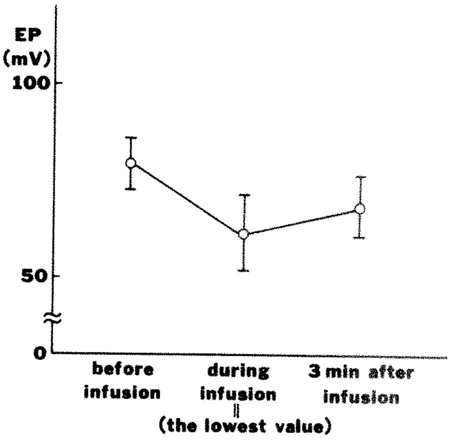

Fig 5. Change in endolymphatic DC potential (EP) associated with 2-μL endolymphatic infusion in 12 guinea pigs.

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The Voice Foundation will sponsor a state-of-the-art conference on Spastic Dysphonia, to be held July 20, 1991, at the Warwick Hotel in Philadelphia, Pennsylvania. For further information, contact The Voice Foundation, 1721 Pine Street, Philadelphia, PA 19103; (215) 735-7999.

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The 26th Postgraduate Course in Ear Surgery will be held from April 7-12, 1991, in Nijmegen, the Netherlands. For further information and registration form, please write to Prof Dr P. van den Broek, University Hospital Nijmegen, Department of Otorhinolaryngology, PO Box 9101, 6500 HB Nijmegen, the Netherlands; Telefax 80-540251.

Ann Otol Rhinol Laryngol 100:1991

IMAGING CASE STUDY OF THE MONTH

SUPERFICIAL SIDEROSIS OF THE CENTRAL NERVOUS SYSTEM

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LOS ANGELES, CALIFORNIA

Otolaryngologists are often confronted with cases of progressive sensorineural hearing loss or dizziness that defy easy characterization. Neurosyphilis, allergy, multiple sclerosis, and autoimmune hearing loss are a few of the diagnoses considered in these difficult cases. We describe the radiographic findings of a rare entity that should also be considered in the differential diagnosis of progressive sensorineural hearing loss or dizziness. Superficial siderosis of the central nervous system is characterized by both intracellular and extracellular deposition of hemosiderin in the leptomeninges, subpial tissue, spinal cord, and cranial nerves.[1] Previously, the diagnosis could only be made at postmortem examination; this fact may account for the relative scarcity of case reports in the literature. With magnetic resonance imaging (MRI) it is now possible to make the diagnosis of superficial siderosis noninvasively.[2,3]

CASE REPORT

A 63-year-old man was initially seen in 1977 with the chief complaint of a progressive hearing loss. Audiometric examination demonstrated a mildly asymmetric high-frequency sensorineural hearing loss with good speech discrimination (right: 10 dB at 500 Hz, 10 dB at 1,000 Hz, 30 dB at 2,000 Hz, 60 dB at 4,000 Hz, speech discrimination score 96%; left: 5 dB at 500 Hz, 5 dB at 1,000 Hz, 20 dB at 2,000 Hz, 45 dB at 4,000 Hz, speech discrimination score 100%). Polytomography of the temporal bones at initial evaluation and cranial computed tomography (CT) and gas-CT cisternography in 1987 revealed normal findings. Subsequently, he has had continued progression of his hearing loss to the point of bilateral total deafness. He also developed a progressive imbalance, but without true vertigo, and diplopia. His neurologic examination 11 years after initial presentation revealed a markedly ataxic, broad-based gait and profound hearing loss (right: speech reception threshold 95 dB, speech discrimination score 12%; left: speech awareness threshold 110 dB [vibrotactile], speech discrimination score 0%) but no other abnormal findings.

Magnetic resonance imaging showed marked abnormalities on intermediate and T2-weighted images. There was low signal intensity surrounding the brain stem, sylvian fissures, anterior longitudinal fissure, and retrothalamic, quadrigeminal, and ambient cisterns, as well as the optic tracts and the acoustic nerves (see Figure).

DISCUSSION

Superficial siderosis (also called pial siderosis) is caused by deposition of hemosiderin in the leptomeninges and subpial tissue from chronic capillary or venous subarachnoid hemorrhage.[1,4,5] It should not be confused with systemic hemochromatosis, which is due to the overloading of the bloodstream with breakdown products of red blood cells and results in the deposition of hemosiderin in the epithelium of the choroid plexus, area postrema, and tuber cinereum but not in the leptomeninges or subpial tissue.[1]

Clinically, the patient may manifest a progressive sensorineural hearing loss, cerebellar dysfunction, pyramidal tract signs, and mental retardation.[1,5-7] The second, fifth, seventh, and eighth cranial nerves are especially vulnerable to the toxic effects of the hemosiderin. In particular, the eighth cranial nerve is especially sensitive to injury by the hemosiderin deposits. The mechanism responsible for this extreme sensitivity is not completely understood. The eighth nerve has the longest glial-lined segment of any cranial nerve, and the severity of injury to a nerve is proportional to the length of the nerve glial segment.[8]

The source of the chronic subarachnoid hemorrhage is identifiable in approximately 50% of autopsied cases.[1] Superficial siderosis is common in posthemispherectomy patients.[1,9] Other sources of recurrent bleeding in reported cases have included papillary ependymomas and neonatal intraventricular hemorrhage.[2,3,10]

The high-field MRI findings are quite characteristic. With use of a 1.5-T magnet, T1-weighted images may appear unremarkable. The T2-weighted images show marked hypointensity of the pial and arachnoid membranes. These areas of hypointensity

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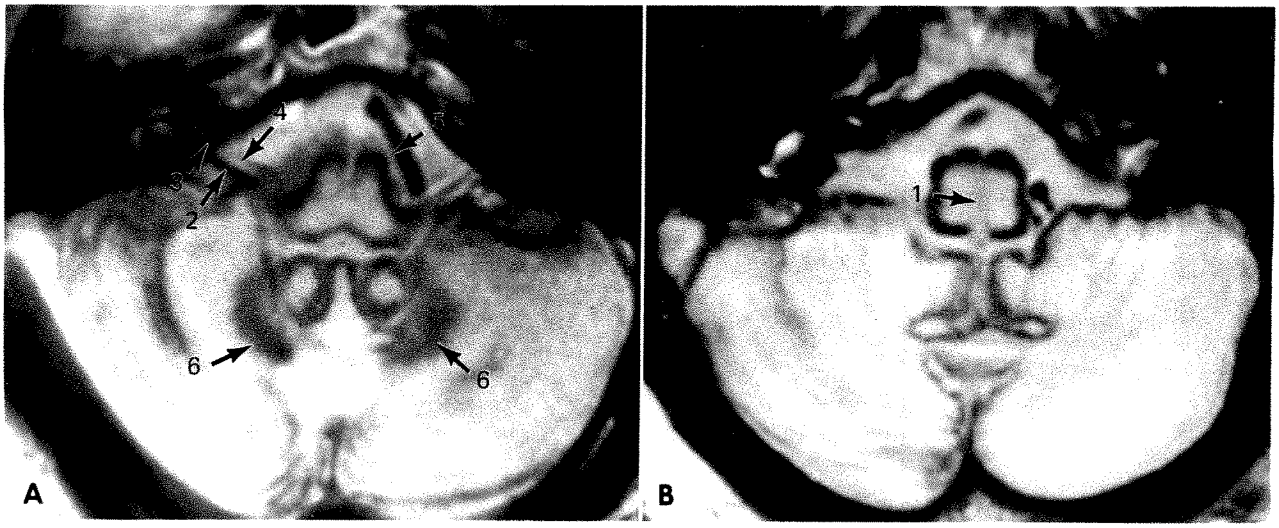
From the Departments of Surgery (Kwartler, De La Cruz) and Radiology (Lo), St Vincent Medical Center; House Ear Clinic (Kwartler, De La Cruz); and St Vincent Radiological Group, Inc (Lo); Los Angeles, California.



Transverse magnetic resonance images at field strength of 1.5 T. A) Intermediate-weighted image (TR/TE = 3,000 ms/30 ms). B) T2-weighted image (3,000/70) 7.5 mm inferior to A. Medulla (1) and cerebellum are outlined by abnormal superficial hypointensity, more pronounced on T2-weighted image than on intermediate-weighted image. Right acoustic nerve (2), seen entering right internal auditory canal (3) posterior to facial nerve (4), is also hypointense and abnormal. Because of tilting of patient's head, left internal auditory canal and vestibulocochlear apparatus are not included on this section. Left facial and acoustic nerves are incompletely imaged. Left vertebral artery is prominent (5). Hypointensity of dentate nuclei (6), however, is physiologic.

correspond to the areas of yellow to rusty brown staining caused by hemosiderin deposition that have been seen grossly at autopsy. Microscopically, most of the pigment is contained within macrophages, with a small portion of staining caused by iron-positive particles in astrocytes.[1,10]

A similar pattern of hypointensity on T2-weighted images has been observed at the periphery of aging intracerebral hematomas.[2] This condition can often be differentiated from superficial siderosis by its localized nature. The hypointensity on T2-weighted images of the dentate nuclei and other extrapyramidal gray matter is not characteristic of superficial siderosis, and represents physiologic iron that increases with age.[2]

Leptomeningeal enhancement of postcontrast CT may be seen in association with superficial siderosis, but is a nonspecific finding and does not necessarily represent siderosis itself.[11]

CONCLUSION

Superficial siderosis may cause a host of symptoms, including progressive audiovestibular dysfunction. It should be considered in the differential diagnosis of unexplainable progressive sensorineural hearing loss and dizziness. Diagnosis can now reliably be made with MRI.

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PATHOLOGY CONSULTATION

TERMINAL DUCT ADENOCARCINOMAS OF SALIVARY TISSUES

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Terminal duct adenocarcinoma is recommended as an encompassing diagnostic designation for a preponderantly intraoral salivary gland carcinoma that has also gone under the names of polymorphous low-grade adenocarcinoma, lobular carcinoma, and low-grade papillary adenocarcinoma. The carcinoma is biologically low grade, with its papillary phenotype manifesting a more aggressive behavior than nonpapillary forms.

Within a short reporting time frame several investigators[1-4] have independently described a low-grade salivary adenocarcinoma that has a strong predilection for the oral cavity, particularly the palate (Tables 1[5-7] and 2[1,8]). In the telling of the adenocarcinoma's clinicopathologic features, it has been given different names: terminal duct adenocarcinoma, lobular carcinoma, polymorphous low-grade adenocarcinoma, and low-grade papillary adenocarcinoma. Three of these are largely descriptive; the other, terminal duct adenocarcinoma, has histogenetic implications and is conceptually unifying. The descriptive terminology, nonetheless, points to the diversity of histologic expression manifested by the carcinoma.

TABLE 2. SALIVARY TUMORS OF PALATE

Histopathologic Type	*Tumors* *No.*	*%*	*Percent of Total*
Benign	730		52
Pleomorphic adenoma	667	91.0	
Others	63	9.0	
Malignant	670		48
Adenoid cystic carcinoma	293	44.0	
Adenocarcinoma	172	26.0	
Mucoepidermoid carcinoma	138	20.5	
Carcinoma ex pleomorphic adenoma	49	7.0	
Acinic cell carcinoma	10	1.4	
Undifferentiated carcinoma	7	1.0	
Miscellaneous	1	0.1	

From data collected by Batsakis et al[1] and Waldron et al.[8]

Whether the low-grade papillary adenocarcinoma is a separate and unrelated neoplasm is arguable, especially since papillary formations are found in other so-called nonpapillary terminal duct adenocarcinomas.[4,9] It is our belief that the low-grade papillary adenocarcinoma lies within the spectrum of histologic expression of terminal duct adenocarcinomas. A papillary configuration, however, does impart a more aggressive behavior (Table 3[5-7]). Reasons for this are not evident from histologic, electron optic, or immunocytochemical studies.[7,10] Slootweg and Müller's[9] data indicate the papillary carcinomas have a greater predilection for the hard palate and are larger than nonpapillary terminal duct adenocarcinomas (median of 2.7 cm versus 2.0 cm), but these factors would not seem to be accountable for biologic differences. Perineural and perineurial invasion are almost constant findings in either type of the carcinoma. A targetlike alignment of neoplastic cells in and around small nerves is very characteristic of the nonpapillary terminal duct adenocarcinomas (see Figure, A). Situated close to bone, the carcinomas have a notable ability to invade the bone (mandible, maxilla) irrespective of type.

Under any designation the carcinoma(s) is a low-grade malignancy. There is general agreement that the adenocarcinomas follow a more favorable clinical course than do adenoid cystic carcinomas.[1,5,9,11]

TABLE 1. TERMINAL DUCT ADENOCARCINOMA OF ORAL CAVITY

Site	*No.*
Palate (soft, hard, and junction)	67
Buccal mucosa	16
Labial mucosa	6
Retromolar area	6
Base of tongue	4
Anterior mandible	1
Total	100

From data reported by Mitchell et al,[5] Anderson et al,[6] and Gnepp et al.[7]

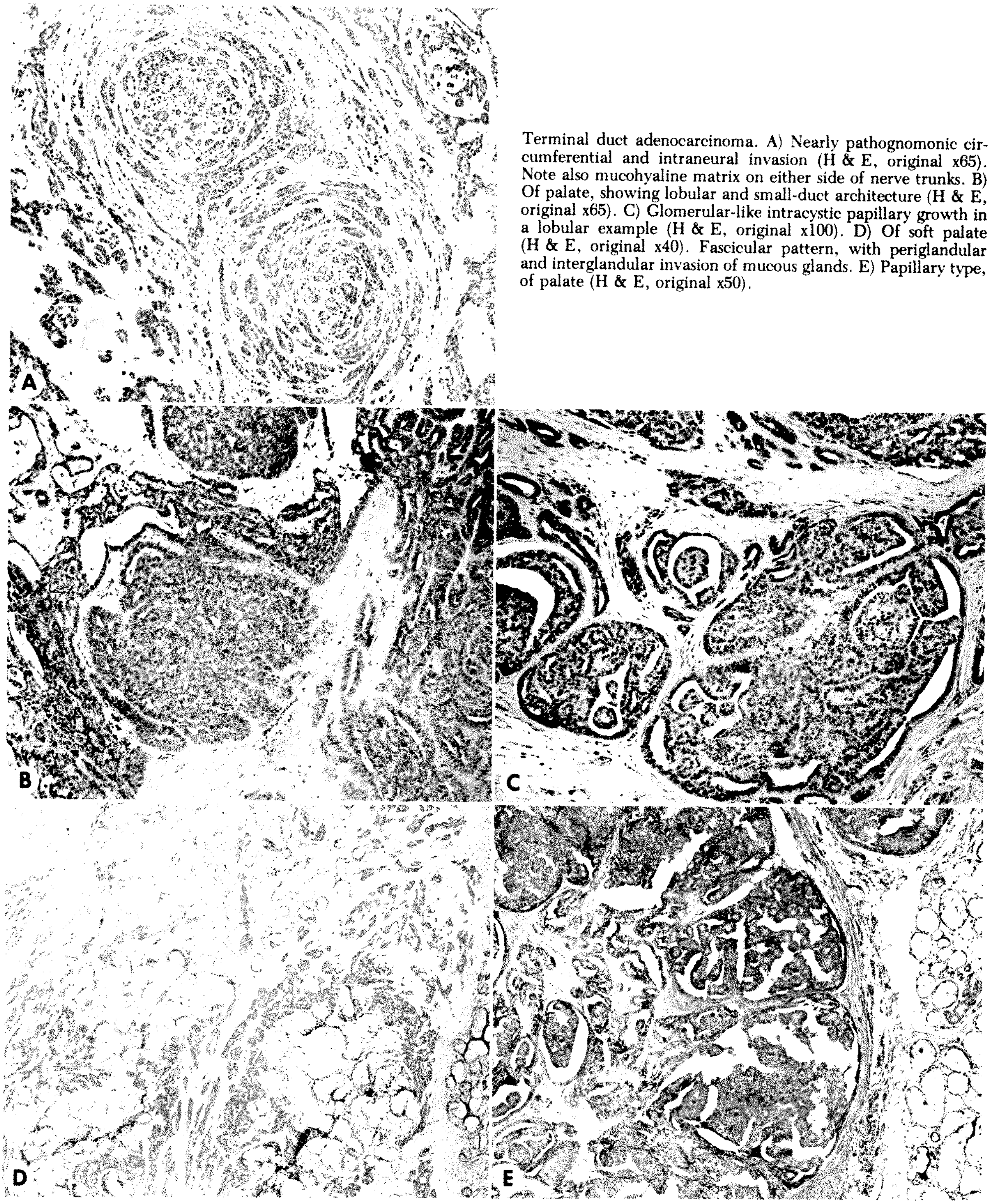
TABLE 3. TERMINAL DUCT ADENOCARCINOMA

	Nonpapillary	*Papillary*	*Total*
Number of patients	86	15	101
Recurrence at primary site	15 (17.4%)	7 (46.6%)	22 (21.8%)
Metastasis to cervical lymph node	6 (6.9%)	6 (40%)	12 (11.9%)
Distant metastasis	0	1 (6.6%)	1 (0.9%)
Death due to carcinoma	1 (1.2%)	2 (13.3%)	3 (2.9%)

From data reported by Mitchell et al,[5] Anderson et al,[6] and Gnepp et al.[7]

From the University of Texas M. D. Anderson Cancer Center, Houston, Texas.

REPRINTS — John G. Batsakis, MD, Dept of Pathology, University of Texas M. D. Anderson Cancer Center, 1515 Holcombe Blvd, Houston, TX 77030.



Terminal duct adenocarcinoma. A) Nearly pathognomonic circumferential and intraneural invasion (H & E, original x65). Note also mucohyaline matrix on either side of nerve trunks. B) Of palate, showing lobular and small-duct architecture (H & E, original x65). C) Glomerular-like intracystic papillary growth in a lobular example (H & E, original x100). D) Of soft palate (H & E, original x40). Fascicular pattern, with periglandular and interglandular invasion of mucous glands. E) Papillary type, of palate (H & E, original x50).

The time interval from first surgical removal to recurrence, in either papillary or nonpapillary terminal duct adenocarcinomas, is characteristically delayed (1 to 20 years). So, too, are the infrequent metastases to cervical lymph nodes: 12 years is the longest interval for this event in our experience.

A cellular blandness with considerable histologic variety characterizes the terminal duct adenocarcinomas. In the nonpapillary forms the cells are small to medium-sized and often have pale, vesicular nuclei resembling those in papillary carcinoma of the thyroid gland (see Figure, B). Larger cells are found in papillary forms. Notable mitotic activity and necrosis are unusual. Intratumoral and stromal hemorrhage may be conspicuous. The stroma ranges from a fibrous, loose vascular character to mucohyaline and hyalinized. Intralesional calcification with calcospherites, luminal crystalloids, and eosinophilic spherules can be seen in either papillary or nonpapillary types.

Terminal duct adenocarcinomas have several growth patterns: lobular (see Figure, C), fascicular (see Figure, D), trabecular, papillary (see Figure, E), ductal, and solid. While one may dominate the histologic appearance, two or more with transitions usually coexist. Fasicular, lobular, and small ductal growth are characteristic of nonpapillary types. Papillary terminal duct adenocarcinomas are rarely purely papillary. Solid, ductal, and trabecular patterns are the usual accompanying architectures. Fascicular growth is not seen in the carcinomas with a preponderant papillary pattern.

The terminal duct adenocarcinoma is only rarely found outside of the oral cavity. In the major salivary glands, however, it can be a form of carcinoma ex pleomorphic adenoma, and it behaves in a far less aggressive manner than its large-duct counterparts.[12]

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NEUROLARYNGOLOGY SYMPOSIUM

A Neurolaryngology Symposium will be held on July 21, 1991, at the Warwick Hotel in Philadelphia, Pennsylvania. For further information, contact The Voice Foundation, 1721 Pine St, Philadelphia, PA 19103; (215) 735-7999.

COMBINED OTOLARYNGOLOGICAL SPRING MEETINGS

1991 Preliminary Programs

(Subject to change and Council approval)

Hyatt Regency Waikoloa, Hawaii

AMERICAN NEUROTOLOGY SOCIETY

Friday, May 3 (all day); Saturday, May 4 (morning); Sunday, May 5 (afternoon)

The William F. House Lectureship: Myth in neurotology. H. F. Schuknecht, MD

Childhood acoustic neuromas. D. R. Maceri, MD; T. Chen, MD; J. G. McComb, MD; S. Giannotta, MD

Selection criteria for hearing preservation acoustic tumor surgery. C. A. Mangham, MD

Decline in hearing after preservation in acoustic tumor surgery. M. J. McKenna, MD; J. B. Nadol, Jr, MD; W. Montgomery, MD; R. Ojemann, MD; R. Levine, MD; C. Halpin, PhD

Cochlear implants in the management of bilateral acoustic neuromas. D. Kohan, MD; N. L. Cohen, MD; R. A. Hoffman, MD

Restoration of binaural hearing with the Audiant implant following acoustic neuroma surgery. J. L. Pulec, MD

Control of patulous eustachian tube symptoms with a new nasal medication. J. R. DiBartolomeo, MD; D. F. Henry, PhD

Correlation of the nerve excitability test with electroneurography in acute facial paralysis. N. J. Coker, MD; J. O. Fordice; S. Moore

A clinical grading scale for and computerized quantitative analysis of synkinesis. J. G. Neely, MD; J. Y. Cheung, PhD; M. Wood, MD

Three-dimensional CT scan reconstruction for the assessment of congenital aural atresia. J. C. Andrews, MD; N. J. Mankovich, PhD; Y. Anzai, MD; R. Lufkin, MD; B. Jabour, MD

A study of recurrence rates of acoustic neuroma in hearing preservation surgery. D. Schessel, MD, PhD; J. Nedzelski, MD; D. Rowed, MD; E. E. Kassel, MD

The use of tissue-integrated prostheses in the rehabilitation of aural atresia. J. K. Niparko, MD; A. W. Langman, MD

Temporal bone histopathology in patients with Nucleus multichannel cochlear implant. H. A. Jenkins, MD; M. A. Marsh, MD; N. J. Coker, MD

Studies of otoacoustic emissions in children with normal ear middle-ear dysfunction and ventilating tubes. J. J. Ownes, MD; M. J. McCoy, MS; B. L. Lonsbury-Martin, PhD; G. K. Martin, PhD

The effect of inner ear pressure change on middle ear mechanics. S. Murakami, MD; R. L. Goode, MD

Differential diagnosis of virus-like particles in the human inner ear. P. A. Wackym, MD; I. S. Storper, MD; S.-F. Yao, MD; W. F. House, MD; P. H. Ward, MD

Ultrastructural changes in the vestibulo-ocular neurons after commissurotomy. R. R. Gacek, MD; A. Kuruvilla, MD; J. E. Schoonmaker

Utility of headshake for evaluation during routine ENG testing. J. A. Goebel, MD

Adaptive plasticity in patients with bilateral vestibular paresis. D. M. Moores, MD; L. F. Hoffman, PhD; K. Beykirch; R. W. Baloh, MD; V. Honrubia, MD

Vestibular and balance testing in ototoxic patients. L. A. Harker, MD; D. G. Cyr, PhD

Mechano receptor disorders of the vestibular system. H. F. Schuknecht, MD

Considerations in the treatment of autoimmune inner ear dysfunction. J. R. E. Dickins, MD; S. S. Graham, MS

Aspartame and dizziness: a prospective, non-blinded cross-over and prevalence study. Preliminary results. A. J. Gulya, MD; R. B. Sessions, MD; M. S. Morris, MD; T. A. Troost, MD; C. P. Hudkins, MD

Labyrinthotomy with streptomycin infusion for vertigo: early results of a multicenter study. E. M. Monsell, MD, PhD; C. Shelton, MD; members of the LSI Multicenter Study Group

Luetic endolymphatic hydrops: diagnosis and treatment. V. S. Dayal, MD; C. A. Amenta III, MD; J. Flaherty, MD; R. J. Weil, MD

Singular neurectomy update II: a review of 102 cases. R. R. Gacek, MD

Retrolabyrinthine vestibular nerve section: an evaluation of technical modification in 164 cases. C. D. Nguyen, MD; W. E. Hitselberger, MD; F. H. Linthicum, MD; D. E. Brackmann, MD

Spontaneous cerebrospinal fluid (CSF) otorrhea. D. G. Pappas, Jr, MD; R. Hoffman, MD; N. L. Cohen, MD; D. G. Pappas, Sr, MD

Microfiberoptic evaluation of the middle ear cavity. I: J. Magnan, MD; A. Chays, MD; D. Gignac, MD. II: D. Edelstein, MD; S. Parisier, MD; S. Bushkin, MD; R. Isaacs, MD; J. Han, MD

Evaluation of perilymphatic fistulas by middle ear exploration. D. S. Poe, MD; E. E. Rebeiz, MD; M. M. Pankratov, MS

Oval window perilymph fistula. Is surgery beneficial? J. B. Farrior, MD; A. C. Sutherland, MS

Retrolabyrinthine-transtentorial approach to lesions of the anterior cerebellopontine angle. S. E. Kinney, MD; G. B. Hughes, MD; J. R. Little, MD

A new bone graft substitute for skull base surgery: an experimental study. B. P. Robinson, MD; E. H. Szachowicz, MD, PhD; J. Hollinger, DDS, PhD

AMERICAN LARYNGOLOGICAL ASSOCIATION

Saturday, May 4 (all day); Sunday, May 5 (afternoon)

Clinical staging for supraglottic cancer. R. L. Zamora; J. E. Harvey, PhD; D. G. Sessions, MD; E. L. Spitznagel, Jr, PhD

Understaging early supraglottic cancer: the pre-epiglottic space considered. S. M. Zeitels, MD; J. A. Kirchner, MD; C. W. Vaughan, MD

Prognostic significance of tumor site and extension in laryngeal cancer. M. D. Morrison, MD; A. D. Flores, MD; A. Sikand, MD; J. S. Durham, MD

Routine endoscopy for head and neck cancer patients. B. H. Haughey, MB, ChB; G. A. Gates, MD

Head and neck surveillance program for factory personnel exposed to asbestos. S. M. Parnes, MD

Carcinoma-in-situ and microinvasive squamous cell carcinoma of the vocal cords. R. E. Rothfield, MD; E. N. Myers, MD; J. T. Johnson, MD

Head and neck cancer: surgery or irradiation? A new consideration. W. F. McGuirt, MD; R. S. Feehs, MD; M. G. Bond, PhD; H. L. Strickland, DVM; W. M. McKinney, MD

Microvascularization of the laryngeal cartilages and its oncological importance. M. Andrea, MD

Seventeenth Daniel C. Baker, Jr, Lecture

In situ hybridization technique in papillomas of the larynx. F. Rimell, MD; R. Maisel, MD; T. Casey, MD; R. Anderson, MD

A study of collagen in the developing human larynx. M. E. Nimni, PhD; S. R. Cohen, MS, MD; V. Mahnovsky, MD

Strobovideolaryngoscopy: results and clinical value. R. T. Sataloff, MD, DMA; J. R. Spiegel, MD; M. J. Hawkshaw, RN

Objective analysis of videostroboscopic images in human vocal cord paralysis. J. A. Sercarz, MD; D. Arnstein, MD; G. S. Berke, MD; M. Natividad; B. R. Gerratt, PhD

Bilateral vocal cord motion impairment (BVCMI): objective evaluation of upper airway obstruction before and after corrective operation. H. K. Kashima, MD

Stroboscopy for glottic T1a carcinomas. Its role in diagnosis. M. Hirano, MD; R. Zhao, MD; S. Tanaka, MD; K. Sato, MD

Open slope quotient: an estimator of glottic resistance. D. H. Slavit, MD; T. V. McCaffrey, MD, PhD; E. Yanagi, MD

Thyroarytenoid intramuscular pressures. D. S. Cooper, PhD; E. Pinczower, MD; D. H. Rice, MD

Multichannel electromyographic observations in spasmodic dysphonia patients and normal control subjects. S. D. Schaefer, MD; R. Roark, PhD; B. Watson, PhD; F. Freeman, PhD; R. Bucher, MS; K. Pool, MD; L. Close, MD; T. Finitzo, PhD

Voluntary control of the soft palate in phonation. E. Yanagisawa, MD; J. Estill, MA; L. Mambrino, MD; D. Talkin

A noninvasive technique to determine vocal efficiency. M. C. Bard, MD; T. V. McCaffrey, MD; D. H. Slavit, MD; R. J. Lipton, MD

Surgical anatomy of the pharyngeal plexus and its role in alaryngeal speech. M. I. Singer, MD; C. E. Shinabarger, MD

The free jejunal graft: effects of longitudinal myotomy on contractility. J. Forsen, MD; B. H. Haughey, MB, ChB

The effect of blood on the incendiary properties of endotracheal tubes irradiated with carbon dioxide laser. R. H. Ossoff, MD; D. A. Gonzalez, MD

An anatomical approach to botulinum toxin injection for the treatment of spasmodic dysphonia. D. C. Green, MD; G. S. Berke, MD; P. H. Ward, MD

Medialization laryngoplasty and the arytenoid adduction procedure: which and when? J. A. Koufman, MD

Physiologic assessment of arytenoid adduction. N. E. Maragos, MD; D. H. Slavit, MD

Collagen injection in the larynx: a report of 166 cases. C. N. Ford, MD; D. M. Bless, PhD; J. M. Loftus, MD

Stable internal fixation of fractures of the thyroid cartilage. J. R. Austin, MD; R. B. Stanley, MD, DDS; D. S. Cooper, PhD

Lidocaine effects on the laryngeal chemo-, mechano- and afferent electrical stimulation reflexes. T. M. McCulloch, MD; P. W. Flint, MD; M. J. Bishop, MD; M. A. Richardson, MD

Synkinesis following reinnervation in the rat; a neuroanatomic and physiologic study using retrograde fluorescent tracers and electromyography. P. W. Flint, MD; D. Downs, MD; M. Coltrera, MD

The characteristics of late responses to superior laryngeal nerve stimulation in humans. C. L. Ludlow, PhD; J. Koda, MD; R. Van Pelt, MD

Electrophysiological investigation of lower cranial nerve diseases by means of magnetic stimulation neuromyography of the larynx. W. F. Thumfart, MD; C. Pototschnig, MD; H. E. Eckel, MD

The three bellies of the cricothyroid muscle. L. Zaretsky, MD; I. Sanders, MD; H. F. Biller, MD

Management of airway obstruction in patients with congenital heart defects. D. Davis, MD; J. A. Tucker, MD; P. Russo, MD

Epiglottis prolapse causing airway obstruction. P. Woo, MD

Special instruments for laryngeal framework surgery. N. Isshiki, MD; H. Kojima, MD; M. Sawada, MD

Teflon injection for vocal cord paralysis. H. H. Dedo, MD

Complications of ethmoid sinus surgery. Occurrence and avoidance. A. J. Sogg, MD; B. S. Eichel, MD

Congenital lack of olfactory ability. D. Leopold, MD; D. Hornung, PhD

AMERICAN BRONCHO-ESOPHAGOLOGICAL ASSOCIATION

Sunday and Monday, May 5-6 (mornings)

Dysphagia following extensive oral cancer surgery. M. Hirano, MD

Endoscopic laser resection of early (T1) laryngeal carcinoma. W. F. McGuirt, MD; D. Blalock, MS; J. Koufman, MD; R. Feehs, MD

Vestibulectomy. An adjuvant in management of T1-T2 vocal cord carcinoma. H. K. Kashima, MD

Percutaneous endoscopic gastrostomy in the management of head and neck carcinoma. S. Gibson, MD; B. L. Wenig, MD

Airway complications of percutaneous endoscopic gastrostomy in head and neck cancer patients. M. Strauss, MD; D. A. Riley, MD

Quantitative mapping of the effect of botulinum toxin injections in the thyroarytenoid muscle. E. F. George, MS; M. S. Zimbler; B. Wu, MD; H. F. Biller, MD; I. Sanders, MD

Histopathologic correlates of time based survival in a transplanted rat allograft. M. Strome, MD; S. Strome; G. Brodsky, MD

Animation of laryngeal embryology: introduction of a powerful educational tool. A. Aly, MD; R. H. Ossoff, MD

Continuous positive airway pressure promotes laryngospasm during halothane anesthesia. D. A. Silva, MD; I. Sanders, MD; M. Munier, MD; F. Rao, MD

Tracheobronchial obstruction from esophageal cancer bronchoscopic treatment with Nd:YAG laser. J. F. Beamis, MD; K. Vergos, MD; E. Rebeiz, MD; S. Shapshay, MD

New modalities in treatment for early laryngeal carcinoma. Panel. C. W. Cummings, MD (moderator); C. T. Yarington, MD; R. Ossoff, MD; A. Hillel, MD (panelists)

Lowered complication rates associated with bronchial foreign bodies (BFB's) over the last 20 years. D. V. Wagner, MD; A. F. Inglis, Jr, MD

Conservative medical management of traumatic pharyngoesophageal perforations. S. Dolgin, MD; A. J. Maniglia, MD; N. Kumar, MD

Investigation of impaired mucociliary (MCT) clearance by the bronchoscopic application of radioactive materials. J. K. Trask, MD; E. L. York, MD; H. Idikio, MD; S. F. P. Man, MD

The effect of reflux and mucosal damage on a rabbit model of subglottic stenosis. D. Albert, FRCS; P. Conn, MBBS; R. Cotton, MD

Pediatric head and neck manifestations of gastroesophageal disease. D. M. Burton, MD; S. M. Pransky, MD; R. Katz, MD

The role of open esophagoscopy in today's fiberoptic world. C. K. Bacon, MD; R. A. Hendrix, MD

Indications and complications of rigid bronchoscopy in the intensive care nursery. H. Girdhar-Gopal, MD; D. Zwillenberg, MD; M. Fucci, MD

Future of medical education in the United States. M. Johns, MD

Comparison of new telescopic video-microlaryngoscopic and standard microlaryngoscopic techniques. E. Yanagisawa, MD; K. Yanagisawa, MD

Measles croup revisited. The Children's Hospital of Los Angeles experience. D. Crockett, MD; E. Kentra-Gorey, MD; W. Mason, MD; L. Ross, MD

Pediatric trans-bronchial lung biopsy. H. R. Muntz, MD; M. S. Wallace, MD

Treatment of tracheal and endobronchial lesions with KTP laser. R. F. Ward, MD

Foreign body injury. A persistent national problem. M. A. Walter, MD; J. S. Reilly, MD

Tracheobronchomalacia. New endoscopic evaluation techniques for a not so uncommon anomaly. E. A. Mair, MD; D. S. Parsons, MD; B. Benjamin, FRACS

Tracheal agenesis. P. J. Koltai, MD; R. Quiney, MB, FRCS

Severe sleep apnea associated with primary bronchotracheomalacia. J. Valentino, MD; R. H. Maisel, MD; M. Mahowald, MD

Ventilation in the dog using a balloon-tipped catheter. D. T. DuBose, MD; R. M. Odland, MD

Thyroid paraganglioma: laryngeal and tracheal invasion. R. E. Brownlee, MD; W. W. Shockley, MD

Granular cell tumor of the subglottic airway with extensive invasion of cartilage. J. J. Moffitt, MD; F. E. Marchant, MD; D. A. Zwillenberg, MD

AMERICAN OTOLOGICAL SOCIETY, INC
Sunday and Monday, May 5-6 (mornings)

Unpublished letters from Prosper Meniere. D. G. Pappas, MD; M. G. McGuinn

Slow motility of outer hair cells. J. Schacht, PhD

Changes in hyaluronan synthesis by in-vitro cultured endolymphatic sac cells. R. A. Schindler, MD; C. P. Amoils, MD; D. Parker, FRCS; G. Hradek

A description of an anterior inferior cerebellar arterial network supplying the rat cochlea. M. D. Seidman; W. S. Quirk; J. M. Miller, PhD

Audiologic profiles of children with acute Kawasaki disease. R. P. Sundel, MD; S. S. Cleveland, MEd; R. E. Novak, PhD; S. Kramer, PhD; J. W. Newburger, MD, MPH; G. Koren, MD; T. McGill, MD; J. P. Harris, MD, PhD; J. C. Burns, MD

Aberration of the tissue collagenase system in association with otosclerosis. M. A. Gorden, MD; J. R. McPhee, PhD; T. R. Van De Water, PhD; R. J. Ruben, MD

Hereditary giant platelet disorder with associated progressive deafness. H. Brodie, MD; R. Chole, MD

Histopathologic and ultrastructural changes in the temporal bones of HIV-infected human adults. S. S. Chandrasekhar, MD; H. K. Chandra Sekhar, MD; V. Siverls, MS

Large cerebellopontine angle meningioma; removal via the transcochlear transtentorial approach. B. A. Thedinger, MD; M. E. Glasscock III, MD; R. A. Cueva, MD: C. G. Jackson, MD

Electrical evaluation of the facial nerve in acoustic neuroma patients. A comparison between transcranial magnetic coil stimulation and electroneurography. L. C. Duckert, MD; D. Hoehmann

Computerized quantitative dynamic analysis of facial motion in the normal and paralyzed face. J. G. Neely, MD; J. Y. Cheung, PhD; M. Wood, MD

Facial nerve management of temporal bone hemangiomas. T. L. Eby, MD; U. Fisch, MD; M. S. Makek, MD

The anatomical importance of the retrofacial air tract. J. E. Benecke, Jr, MD; A. Kuczer, MD

A grading system for the selection of patients with congenital aural atresia. R. A. Jahrsdoerfer, MD; J. W. Yeakley, MD; L. C. Gray, PhD; E. A. Aguilar, MD

Tinnitus: a study of the effect of acoustic tumor removal. C. Shelton, MD; K. Berliner, PhD; W. E. Hitselberger, MD

Longitudinal evaluation of communication skills of children with single- or multi-channel cochlear implants. R. T. Miyamoto, MD; M. J. Osberger, PhD; A. M. Robbins, MD; W. A. Myres, MAT; K. Kessler, MD

The effects of active channel number and place of stimulation on performance with multi-channel cochlear implant. P. R. Kileny, PhD; S. Zimmerman-Phillips, MD; J. L. Kemink, MD; T. A. Zwolan, PhD

The use of sensory aids in conjunction with cochlear implants. S. B. Waltzman, PhD; N. L. Cohen, MD; W. H. Shapiro, MA

Binaural cochlear implants. J. D. Breen, Jr, MD; W. M. Luxford, MD; L. L. Tonokawa, MS; B. A. Bell, MA

Trends in education of hearing-impaired children. P. Stone

Neural presbycusis: a diagnostic dilemma. G. A. Gates, MD; G. R. Popelka, PhD

Hearing results from endolymphatic sac surgery. D. W. Goin, MD; B. A. Esses, MD; D. P. Hill, MD; R. E. Mischke, MD

Chemical labyrinthectomy: local application of gentamicin for the treatment of unilateral Meniere's disease. D. A. Schessel, PhD, MD; J. M. Nedzelski, MD; G. E. Bryce, MD; A. G. Pfleiderer, MD

Vestibular neurectomy in the USA — 1990. H. Silverstein, MD; S. Rosenberg, MD; J. Planzer, MD; H. Wanamaker, MD

AMERICAN LARYNGOLOGICAL, RHINOLOGICAL AND OTOLOGICAL SOCIETY, INC

Tuesday to Thursday, May 7-9 (mornings)

The learning curve in stapes surgery. G. B. Hughes, MD

Long term results of mastoid cavities grafted with cultured epithelium prepared from autologous epidermal cells to prevent chronic otorrhea. D. J. Premachandra, FRCS; B. Woodward, PhD; C. M. Milton, FRCS; R. J. Sergeant, FRCS; J. W. Fabre, MB, BS, PhD

Perilymph fistula: the Warren Otologic Group experience. F. M. Rizer, MD; W. H. Lippy, MD; A. G. Schuring, MD; A. McGill Smith, BSN

Perilymph fistula: review of 260 exploratory tympanotomies. D. C. Kelsall, MD; R. E. Mischke, MD; D. W. Goin, MD

Noise induced hearing loss in childhood. P. E. Brookhouser, MD

Otoacoustic emissions in normal and hearing impaired children and normal adults. Z. Spektor, MD; G. Leonard, MD; D. O. Kim, DSc; M. D. Jung, MS; J. Smurznski, PhD

Management of cholesteatoma in children. M. A. Fazekas-May, MD; S. J. Stern, MD

A new concept for implantable hearing aids. S. Gilman, PhD; J. W. House, MD; J. P. Mobley, MSEE

The effects of endolymphatic duct occlusion on the structure and function of the in vitro cultured, adult guinea pig, endolymphatic sac (ELS). D. A. Parker, FRCS; R. A. Schindler, MD; P. Amoils, MD; G. T. Hradek, MS

Pneumococcal meningogenic hearing loss (MHL): an animal model. S. Mahesh Bhatt, MD; W. Hsu, MD; C. Halpin, PhD; R. A. Levine, MD; E. Tuomanen, MD; B. A. Thedinger, MD; J. B. Nadol, Jr, MD

Preliminary results with the Clarion cochlear implant. R. A. Schindler, MD; D. K. Kessler, MA

Insertional trauma of multichannel cochlear implants. D. B. Welling, MD; B. J. Gantz, MD; R. Hinojosa, MD; J. T. Lee, MD

Receptive and expressive language abilities following cochlear implantation. S. A. Hellman, MS; P. Chute, MA; L. Thurston, MA; S. C. Parisier, MD

The presence of HPV DNA in laryngeal papillomas, squamous cell carcinomas, and their laser vapor. R. M. Rossi, MD; D. Parris, MD; D. E. Schuller, MD

Human papillomavirus identification by DNA in situ hybridization in concomitant nasal papillomas and genital warts. L. A. Hoover, MD; Y. S. Fu, MD; L. Cheng, MS; M. D. Franklin, MD

Early experience with percutaneous tracheostomy. M. B. Wang, MD; G. S. Berke, MD; T. C. Calcaterra, MD; D. Watts, RN

Cardiovascular effects of pseudoephedrine in medically controlled hypertensive patients. R. A. Beck, MD; D. Mercado, MD; S. Seguin, MD; W. P. Andrade, MD; H. Cushner, MD

Effects of botulinum toxin therapy in patients with adductor spasmodic dysphonia: acoustic, aerodynamic and videoendoscopic findings. P. Zwirner, MD; T. Murry, PhD; M. Swenson, MD; G. E. Woodson, MD

Abductor laryngeal dystonia: a series treated with botulinum toxin. A. Blitzer, MD, DDS; M. F. Brin, MD

Vocal function in thyroplasty type I procedure. S. D. Gray, MD; J. Barkmeier, MS; D. Jones, PhD; I. Titze, PhD; C. Shive; D. Drucker

Ogura Lecture. R. W. Cantrell, MD

Functional endoscopic sinus surgery. Experience and observations in a residency teaching program. J. B. Jacobs, MD; P. Gittleman, MD; S. Chandrasekhar, MD

Holmium laser assisted endoscopic sinus surgery. Clinical experience. E. E. Rebeiz, MD; S. Shapshay, MD; M. M. Pankratov, MS

Training in endoscopic sinus surgery: CT analysis of surgical technique in the dissection. W. MacLean, MD; H. C. Moore, MD; G. Geil, MD; F. Kuhn, MD

Maxillary removal and reinsertion for improved access to cranial base tumors. D. E. Schuller, MD; B. L. Brown; K. J. Miller

The treatment of hemangiomas of the head and neck. M. Waner, MD; J. Y. Suen, MD

Laryngeal pathology in non-surviving intubated neonates. T. Joseph, MB; P. Nicklaus, MD; P. Van Nostrand, MD; W. Crysdale, MD

Lyme disease: improved diagnostic protocol. W. J. Mann, MD; R. G. Amedee, MD

The role of neck dissection as a prophylactic procedure in the face of negative imaging. R. Feinmesser, MD; J. L. Freeman, MD; B. Mullen, MD; A. A. Noyek, MD

3-D CT scanning for evaluation of head and neck cancer. M. Friedman, MD; M. Mafee, MD

Technical advances in MR imaging for head and neck cancer. R. D. Tien, MD; J. R. Hesselink, MD; A. M. Berson, MD; K. T. Robbins, MD

Positron emission tomography: a new method in detection of primary tumors of the head and neck and assessing metastatic cervical adenopathy. J. W. Bailet, MD; B. A. Jabour, MD; E. Abemayor, MD; K. B. Briskin, MD

Orbital and cerebral complications of mucormycosis. An experimental model. V. K. Anand, MD; J. A. Griswold, Jr, MD; J. M. Reed, MD

Trends in hyperpararthyroidism surgery. W. Morioka, MD

Successful in-vitro growth of human respiratory epithelium on a tracheal prosthesis. R. C. Kern, MD; P. A. Mathieu; D. P. Chopra, PhD; J. R. Jacobs, MD

Effects of denervation on laryngeal muscles. A canine model. M. L. Shindo, MD; G. D. Herzon, MD; D. G. Hanson, MD; V. Sahgal, MD

Skull base surgery: fact, fad, fringe or fancy? P. J. Donald, MD

Vagal paraganglioma: a report of eight cases. C. Eriksen, MD; L. D. Lowry, MD; H. Girdhar-Gopal, MD

Inferior mastoidectomy-hypotympanic approach to glomus tumors: an anatomic/CT scan study with correlation of distances between critical structures. R. C. Sprecher, MD; A. J. Maniglia, MD; C. Megerian, MD; C. Lanzieri, MD

Acute intraoperative tissue expansion. A histological and clinical correlation. G. R. Holt, MD

Electrophysiologic and histologic effects of the argon beam coagulator on peripheral nerves. J. R. Steiniger, MD; W. E. Fee, MD; K. W. Nowels, MD; H. S. Lusted, PhD; A. Wilkinson, MD

Photodynamic therapy (PDT) for treatment of esophageal cancer. V. Schweitzer, MD

Flutamide-induced regression of angiofibroma. G. A. Gates, MD; D. H. Rice, MD; C. Koopman, MD; D. Schuller, MD

AMERICAN SOCIETY FOR HEAD AND NECK SURGERY

Tuesday to Thursday, May 7-9 (afternoons)

Effectiveness of salvage neck dissection for advanced regional metastases when induction chemotherapy is used for organ preservation in laryngeal cancer. G. T. Wolf, MD; S. Fisher

Selective neck dissection. J. E. Medina, MD; D. Johnson, MD

The pathologic basis of surgery in the management of post-radiotherapy cervical metastasis in nasopharyngeal carcinoma. W. I. Wei, MD; K. H. Lam, MD; S. K. Lau, MD; C. M. Ho, MD; P. Wong, MD; W. F. Ng, MD

Cancer treatment: the basis for current failures and the possibilities of future successes. F. F. Becker, MD

The eleventh nerve syndrome: accessory nerve palsy or adhesive capsulitis? C. Patten, MD; A. Hillel, MD

The significance of false positive nodes in patients with oral cancer. R. J. Baatenburg de Jong, MD, PhD; J. L. Freeman, MD; P. G. Gullane, MD; A. M. Noyek, MD

Standardizing neck dissection terminology: official report of the Academy's Committee for Head and Neck Surgery and Oncology. K. T. Robbins, MD; J. E. Medina, MD; G. T. Wolf, MD; P. A. Levine, MD; R. B. Sessions, MD; C. W. Pruet, MD

Parathyroid exploration: a review of 120 cases. G. W. Summers, DMD, MD

What information should we learn from biopsied material of head and neck cancer? Y. Murakami, MD

Sutureless vascular anastomosis with biocompatible heat-shrink tubing. D. E. Mattox, MD; J. Wozniac, MD

The superior trapezius myocutaneous flap in head and neck reconstruction. J. E. Aviv, MD; M. L. Urken, MD; W. Lawson, MD, DDS; H. F. Biller, MD

The combined latissimus dorsi–scapula free flap in head and neck reconstruction. J. E. Aviv, MD; M. L. Urken, MD; C. Vickery, MD; H. Weinberg, MD; D. Buchbinder, DDS; H. F. Biller, MD

The combined sensate radial forearm and iliac crest free flaps for reconstruction of significant glossectomy-mandibulectomy defects. M. L. Urken, MD; H. Weinberg, MD; C. Vickery, MD; J. Aviv, MD; D. Buchbinder, DMD; W. Lawson, MD, DDS; H. F. Biller, MD

Extensive defects of the sino-orbital region — results with microvascular reconstruction. K. D. Olsen, MD; N. B. Meland, MD; M. J. Ebersold, MD; G. B. Bartley, MD; J. A. Garrity, MD

Mechanisms of lymphocyte-mediated cytotoxicity: early intracellular calcium changes correlate with in vitro cytotoxicity of LAK-sensitive and resistant squamous carcinomas. B. Burkey, MD; G. T. Wolf, MD; G. Oman, MD; J. Poore, MD; D. Hinshaw, MD; T. E. Carey, MD

The effect of hyperbaric oxygen on growth of human squamous cell carcinoma xenografts in nude mice. D. B. Headley, MD; M. Gapany, MD; D. E. Dawson, MD; G. Kruse, MD; R. S. Robinson, MD; B. F. McCabe, MD

Enhancement of tumor infiltrating lymphocyte response in squamous cell carcinoma of the head and neck using a prostaglandin synthesis inhibitor. D. S. Cross, MD; J. L. Platt, MD; S. K. Juhn, MD; F. H. Bach, MD; G. L. Adams, MD

Chemoprevention in head and neck cancer. Panel. W. K. Hong, MD; H. Kashima, MD; S. Schantz, MD; W. Richtsmeier, MD (panelists)

Progesterone receptors in squamous cell carcinoma of the head and neck. D. H. Slavit, MD; N. J. Berg, MD; H. B. Neel III, MD, PhD; J. E. Lewis, MD; T. C. Spelsberg, PhD

Epidermal growth factor receptor amplification in head and neck cancer. T. F. Pingree, MD; A. A. E. El-Zayat, PhD; P. M. Mock, MD; G. M. Clark, PhD; R. A. Otto, MD; D. D. Von Hoff, MD

A study of the heterogeneity of the mucoepidermoid tumor and the implication for future therapies. D. A. Ross, MD; J. A. Huaman, MD; S. H. Barsky, MD

Detection of EBV genomes in nasopharyngeal carcinoma. R. Feinmesser, MD; J. L. Freeman, MD; A. M. Noyek, MD; H. M. Dosch, MD, PhD

Orbital decompression for preservation of vision in Graves' ophthalmopathy. D. Girod, MD; J. C. Orcutt, MD; C. W. Cummings, MD

A new bone graft substitute for head and neck reconstruction: an experimental study. B. Robinson, MD; E. Szachowicz, MD, PhD; J. Hollinger, DDS, PhD

Functional stability and biomechanical strength of canine segmental mandibular defects reconstructed using a recombinant bone-inducing factor. D. M. Toriumi, MD; H. S. Kotler, MD; D. P. Luxenberg; V. Rosen, PhD; E. A. Wang, PhD

Prognostic factors in the recurrence of stage I and II squamous cell cancer of the oral cavity. K. R. Jones, MD, PhD; W. W. Shockley, MD

Accuracy of pathology diagnosis in thyroid lesions. J. Irish, MD; P. Van Nostrand, MD; P. Gullane, MD; S. Asa, MD; L. Rotstein, MD

Reconstruction following skull base resection — analysis of 100 consecutive procedures. V. L. Schramm, Jr, MD

Outcome and complications of anterior craniofacial resection. W. J. Richtsmeier, MD, PhD; R. J. S. Briggs, MD; W. M. Koch, MD; D. W. Eisele, MD; M. Loury, MD; B. S. Carson, MD

Primary squamous cell carcinoma of the parotid gland. R. K. Gaughan, MD; K. D. Olsen, MD

Salivary gland neoplasms in children. D. L. Callender, MD; R. A. Frankenthaler, MD; M. A. Luna, MD; H. Goepfert, MD

Prognostic variables in the treatment of parotid cancer. R. A. Frankenthaler, MD; M. A. Luna, MD; K.-K. Ang, MD, PhD; R. M. Byers, MD; H. Goepfert, MD

Acinic cell carcinoma of the salivary gland: the prognostic relevance of DNA flow cytometry and nucleolar organizer regions. C. Timon, MD; P. Gullane, MD; I. Dardick, MD

Tumor necrosis factor and chemotherapeutic agents: potentiation of cytotoxicity with gamma interferon. D. E. Dawson, MD; M. Gapany, MD; R. C. Burgess, MD; D. B. Headley, MD; P. V. Boeson, MD

4-Nitroquinolone-*N*-oxide carcinogenesis: a mouse model of human oropharyngeal squamous cell carcinoma. B. L. Hawkins, MD; B. W. West, MD; S. A. Martinez, MD; F. J. Hendler, MD, PhD

Elevated levels of serum interleukin-2 receptor and tumor necrosis factor in patients with nasopharyngeal carcinoma. M.-M. Hsu, MD; J.-Y. Ko, MD; Y.-L. Chang, MD

Intratumoral heterogeneity of DNA content in laryngeal squamous carcinoma. A. El-Naggar, MD; M. Luna, MD; L. Garsney, MD; J. Batsakis, MD

Thyroid dysfunction following radiation therapy in the head and neck cancer patient. T. A. Tami, MD; LCDR P. Gomez, MC, USNR; CDR G. S. Parker, MC, USN; M. B. Gupta

Perceptual and acoustic assessment of voice in patients with laser- and radiation-treated T1 vocal cord carcinomas. W. F. McGuirt, MD; D. Blalock, MD; J. A. Koufman, MD; R. S. Feehs, MD

The effect of radiation fraction size on local control rates for early glottic cancer: a model analysis for in vivo tumor growth and radio response parameters. E. J. Ricciardelli, MD; E. A. Weymuller, Jr, MD; W.-J. Koh, MD; M. Austin-Seymour, MD; G. E. Laramore, PhD, MD

Long-term problems of tracheoesophageal puncture patients. R. C. Wang, MD; T. Bui, MD; M. Ditkoff, MD; E. Sauris, MD; V. Anand, MD; I. Klatsky

Intrathecal narcotics for relief of intractable pain from head and neck cancer. P. E. Andersen, MD; J. I. Cohen, MD, PhD; E. E. Everts, MD; M. Bedder, MD; K. Burcheil, MD

Re-evaluation of intra-arterial chemotherapy for advanced head and neck malignancies. K. T. Robbins, MD; A. M. Storniolo, MD; C. W. Kerber, MD; A. M. Berson, MD

Long term results of surgical management of recurrent nasopharyngeal carcinoma after radiation therapy failure at the primary site. W. E. Fee, Jr, MD; J. B. Roberson, Jr, MD; D. R. Goffinet, MD

The influence of intensive hyperbaric oxygen therapy on skin flap survival in a swine model. P. K. Pellitteri, DO; T. L. Kennedy, MD; B. A. Youn, MD

Enhanced survival of skin flaps raised in previously irradiated fields by WR-2721: an experimental study. B. J. Hasslinger, MD; L. A. Kleiman, MD; H. Eddy, PhD; C. M. Suter, PhD; W. C. Gray, MD; C. L. Blanchard, MD

The effect of postoperative radiotherapy on pharyngoesophageal reconstruction with free jejunal interposition. G. J. Petruzzelli, MD, PhD; J. T. Johnson, MD; E. Cano, MD; E. N. Myers, MD; E. J. deVries, MD; R. Wagner

AMERICAN RHINOLOGIC SOCIETY

Wednesday and Thursday, May 8-9 (afternoons)

Secure endoscopic sinus surgery as an adjunct to functional nasal surgery. P. Toffel, MD

Endoscopic middle meatus antrostomy. J. Duncavage, MD

Pediatric endoscopic nasal surgery. C. Gross, MD

Marsupialization in sinus surgery — functional sinus surgery: the myth. W. Friedman, MD

Prognostic features in successful endoscopic revision surgery of the paranasal sinuses. B. D. Ridenour, MD; S. D. Schaefer, MD

Panel on nasal reconstruction. Grafts. G. Shaw, MD; Nasolabial flaps. F. Stucker, MD; Midline forehead flap. J. R. Thomas, MD; Sliding nasal dorsal flap. W. Shockley, MD; Panel discussion. F. Stucker, MD (moderator); J. R. Thomas, MD; W. Shockley, MD; G. Shaw, MD (panelists)

Chronic fatigue of nasal origin. A. Chester, MD

Acute complications of nasotracheal intubation. L. Welsh, MD; J. J. Welsh, MD; L. Roitman, MD

Combined medical/surgical management of the allergic nose. R. Trevino, MD

Nasal resistance, aerobic capacity and athletic performance. M. S. Benninger, MD

Total nasal septal reconstruction with caudal end transplant. D. Slavit, MD; G. W. Facer, MD; E. B. Kern, MD

Allergic rhinosinusitis: the total rhinologic disease. R. Trevino, MD

A personal technique in septal surgery. E. B. Kern, MD

The twisted nose — a practical approach. F. Stucker, MD

AMERICAN SOCIETY OF PEDIATRIC OTOLARYNGOLOGY

Thursday, May 9 (afternoon); Friday and Saturday, May 10-11 (mornings)

Combined electrical and acoustical stimulation in a single bimodal hearing prosthesis. G. M. Clark, PhD, FRACS; G. Dooley, BSc, PhD; P. Seligman, BE, PhD; P. Blamey, BSc, PhD

Perception results in children using the Nucleus 22-channel cochlear implant: a multi-center study. J. B. Firszt, MA; M. A. Novak, MD; L. L. Tonokawa, MS; W. M. Luxford, MD; S. Zimmerman-Phillips, MS; J. L. Kemink, MD; H. Fryauf-Bertschy, MA; B. Gantz, MD

Pathogenesis of otitis media in Palau: an epidemiologic study. K. H. Chan, MD; J. D. Swarts, PhD; R. C. Rudoy, MD; G. J. Dever, MD

Cytokines in middle-ear effusions: interleukin-6 (IL-6). R. F. Yellon, MD; G. Leonard, MD; P. Marucha, DMD; R. Carpenter, MD; J. Burleson, PhD; D. Kreutzer, PhD

A model of the neonatal ear inflammation response. R. D. Eavey, MD; A. Camacho R., MD; C. Northrop

Steroids and otitis media with effusion: meta-analysis of published clinical trials. R. M. Rosenfeld, MD; E. M. Mandel, MD; C. D. Bluestone, MD

Cholesteatoma in children: is destruction of the scutum still a valid sign of disease? E. Al-Zimaiti, MD; M. D. Schloss, MD; A. M. O'Gorman, MD

Cholesteatoma in children: predictors of recurrence and second-look status. R. L. Moura, MD; R. M. Rosenfeld, MD; C. D. Bluestone, MD

The vestibular aqueduct syndrome. D. N. Madgy, DO; W. M. Belenky, MD; J. Leider, MD; A. J. Hotaling, MD

Vestibular and visual-ocular maturation in normal children. G. S. Kenyon, MB, ChB, FRCS

Hereditary inner ear malformations in humans — a classification. R. J. H. Smith, MD; K. P. Steel, PhD; L. Michaels, MD, FRCPath, FRCP(C)

Comparison of autograft and homograft cartilage in experimental laryngotracheal reconstruction. D. M. Albert, FRCS; P. Conn, MRCPath; R. T. Cotton, MD

An in vitro model for studying growth: effects of trauma and external agents on the cricoid at the cellular level. G. H. Zalzal, MD; F. Luyten, MD, PhD

Transplant of long tracheal segments in rabbits. D. M. O'Connor; D. M. Albert, FRCS; D. K. Holmes, MD; P. C. Conn, MD; R. T. Cotton, MD

Effect of extraluminal O2 concentration on ignition of endotracheal tubes by the CO2 laser. J. E. Arnold, MD; A. L. Allphin, MD

Effect of laryngeal stenting on epithelialization of anterior costal cartilage grafts using a goat model. B. J. Wiatrak, MD; D. Albert, MD; D. Holmes, MD; R. T. Cotton, MD

Four quadrant division of the cricoid cartilage in laryngotracheal reconstruction. R. T. Cotton, MD; A. J. Mortelliti, MD; C. M. Myer III, MD

Gastro-esophageal-pharyngeal reflux in children. A pharyngeal pH monitoring study. P. Contencin, MD; P. Narcy, MD

Gastroesophageal reflux (GER) complicating choanal atresia repair. D. J. Beste, MD; S. F. Conley, MD

Pediatric caustic ingestion: a clinical update. R. Boucher, MD; L. W. C. Tom, MD; W. P. Potsic, MD; S. D. Handler, MD; R. F. Wetmore, MD

Swallowing disorders in a population of children with cerebral palsy. E. T. Waterman, MD; P. J. Koltai, MD; A. T. Cacace, PhD; J. C. Downey, CCC-LSP

Vocal function in papilloma patients. S. D. Gray, MD; J. Barkmeier, MS; C. Shive, RN; D. Jones, PhD; D. VanDenmark, PhD

Laryngeal electromyography in infants and children: technique and results. B. R. Maddern, MD; L. J. Dindzans, MD; H. Wessel, MD

Acoustic and perceptual analysis of voice quality following laryngotracheal reconstructon. C. Edmond, MD; M. McClain, PhD; C. Gonzalez, MD; J. H. Nowlin, DDS, MD

Correlation of clinical findings with polysomnography results in children with suspected obstructive sleep apnea. J. Leach, MD; J. Olson, MD; J. Hermann, PhD; S. Manning, MD

Respiratory events after adenotonsillectomy in children with obstructive sleep apnea. S. A. McColley, MD; M. M. April, MD; J. L. Carroll, MD; R. N. Naclerio, MD; G. M. Loughlin, MD

Facial skeletal morphology in children with and without nasal obstruction. D. H. McKibben, DMD, MDS; W. A. Marasovich, MD, DDS; J. L. Paradise, MD; D. K. Colborn; B. S. Bernard, RN, PNP; C. D. Bluestone, MD

Needle aspiration of peritonsillar abscess in children. E. Weinberg, MD; L. S. Brodsky, MD; J. Stanievich, MD; M. Volk, MD, DMD

Congenital nasal pyriform aperture stenosis: isolated abnormality vs developmental field defect. H. Arlis, MD; R. F. Ward, MD

Follow-up of endoscopic sinus surgery on children with cystic fibrosis. J. P. Cuyler, FRCS

Lacrimal drainage system injury during FES: incidence, anatomic analysis and an improved surgical approach to avoid complications. D. S. Parsons, MD; W. E. Bolger, MD; E. A. Mair, MD; F. A. Kuhn, MD

External rhinoplasty approach for rhinologic surgery in children. P. J. Koltai, MD; J. Hoehn, MD; C. M. Bailey, BSc

Preoperative thyroid scanning in presumed thyroglossal duct cysts (TGD cysts). E. F. Pinczower, MD; D. M. Crockett, MD; J. B. Atkinson, MD; S. Kuhn, RN

Importance of CT and MRI scans in pediatric skull base lesions. D. M. Crockett, MD; R. P. Lusk, MD; M. Nelson, MD; H. R. Muntz, MD; W. H. McAlister, MD

Pediatric skull base surgery. V. L. Schramm, Jr, MD; L. Sekhar, MD; L. McCleary, MD

IOWA BASIC SCIENCE COURSE IN OTOLARYNGOLOGY FOR RESIDENTS

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Head and Neck Surgery
The University of Iowa

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AN OPEN LETTER TO PHYSICIANS and SPEECH PATHOLOGISTS

February 28, 1991

TO WHOM IT MAY CONCERN:

At least three views exist about the cause of Spastic Dysphonia: physicians believe the cause is medical; psychiatrists believe it is psychological; and my position as a voice and speech pathologist is that Spastic Dysphonia is caused by misuse and abuse of the speaking voice. It is a mechanical problem, with psychological overtones. The individual is figuratively talking with the brakes on, squeezing the voice from the lower throat, and the breathing is in the wrong gear.

In 1982, at Cedars-Sinai Medical Hospital, Los Angeles, I presented three patients who had confirmed severe Spastic Dysphonia to an audience of Ear, Nose, and Throat doctors. These patients told the audience how they had recovered their speaking voices by Direct Voice Rehabilitation. Henry J. Rubin, a well-known ENT specialist, asked after the presentation: "We know that you are the only one successful by speech therapy. Why?" The answer is, I do not do speech therapy; I do Direct Voice Rehabilitation. Henry J. Rubin, M.D., Associate Professor, Department of Head and Neck Surgery, UCLA School of Medicine, Retired, and Former Chief of the Service of Otolaryngology, Cedars of Lebanon Hospital, Los Angeles, commented in 1990: "In the fifteen years immediately preceding my retirement from the active practice of otolaryngology, I referred my patients in need of Voice Rehabilitation to Dr. Cooper because his results proved to be the most consistently satisfactory. His methods seemed essentially to be quite simple, in fact to the point sometimes of challenging believability, but they worked. He explains these methods in his book, and I believe that any voice therapist who gives them a serious and unbiased trial will be agreeably surprised."

In 1990, I was again invited to return as guest speaker at Cedars-Sinai Medical Center. This time I presented five patients with diagnosed Spastic Dysphonia and discussed how I had helped them with Direct Voice Rehabilitation. Regarding the treatment of Spastic Dysphonia by Direct Voice Rehabilitation in patients seen in his private practice group, a very prominent otolaryngologist, Edward A. Kantor, M.D., Chairman, Division of Otolaryngology, Head and Neck Surgery, Cedars-Sinai Medical Center, Los Angeles, had this to say: "Dr. Morton Cooper has shown unusual expertise in treating patients with Spastic Dysphonia. His methods of voice therapy in our patients afflicted with this markedly disabling disease have been highly successful."

Over the past fifteen years, I have been to meetings of the American Speech-Language-Hearing Association, the California Speech-Language-Hearing Association, and the International Association of Logopedics and Phoniatrics, presenting with tapes or with actual patients the recovery from Spastic Dysphonia by Direct Voice Rehabilitation. In articles and videos (in local TV shows on American Cable and Century Cable) I have reported on "before and after" patients who have had Spastic Dysphonia.

The late Henry Fonda had Spastic Dysphonia. Through a program of Direct Voice Rehabilitation, Mr. Fonda was able to recover his voice and film "On Golden Pond," a movie for which he received an Oscar. Another patient, Dr. Don Dodson said in a Los Angeles Times interview that he had fully recovered from Spastic Dysphonia. Zelda Pollock, who developed Spastic Dysphonia while teaching, went on KCBS to tell about her recovery.

People come from all over the world for my help in resolving Spastic Dysphonia. A professor came from the Middle East, having been directed by a medical doctor in the United States, on an RX form, to "chew on a golf ball." By Direct Voice Rehabilitation, the patient recovered in a year. I have received yearly reports from him; he has never lost his voice again. Jim Johnson, a minister from the Mid-West, having had severe Spastic Dysphonia for almost nine years and trying all kinds of therapy unsuccessfully (even going to the Mayo Clinic), is now talking with a normal voice; he underwent an intensive daily one month program of Direct Voice Rehabilitation with me four years ago. He says his voice recovery is a miracle.

I have found that Spastic Dysphonia, which I call the monster voice, isn't hopeless and that it has had an excellent prognosis in my office. My techniques differ from those of my colleagues, and I am sharply critical of what some of my colleagues and medical associates do for Spastic Dysphonia. Patients with Spastic Dysphonia are usually not given options to surgery and botulinum treatment. The downside of these procedures, I find, is not presented to these patients. Direct Voice Rehabilitation is a holistic, conservative, non-risk, non-invasive and natural way of helping those with Spastic Dysphonia, and patients should be given this as an alternative approach. Are the medical doctors and the speech pathology associations playing the politics of voice?

In 1973, in my textbook, Modern Techniques of Vocal Rehabilitation, I wrote about recovery from Spastic Dysphonia. In my two most recent books, Change Your Voice, Change Your Life and Winning With Your Voice, I discuss the way to get a better, more effective voice, and I detail how those suffering from Spastic Dysphonia have been helped by my Direct Voice Rehabilitation program.

Recently, I was invited to speak at the March program on Spasmodic Dysphonia at UCI Center for Health Education, my topic being "Twenty Years of Success with Spastic Dysphonia by Direct Voice Rehabilitation." Unfortunately, Daniel Truong, M.D. later said there was not enough time for my presentation; therefore, my approach to Spastic Dysphonia was omitted. If you or your organization wish to hear my approach to Spastic Dysphonia, please write 10921 Wilshire Blvd., Ste. 401, Los Angeles, CA 90024 or call 1-800-932-3221.

Sincerely,

Morton Cooper

MORTON COOPER, Ph.D., Speech Pathologist

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